Personal Care Products and Urinary Levels of Phthalates in Mexican women

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Abstract and keywords

Sources of phthalates other than PVC related products are scarcely documented in Mexico. The objective of our study was to explore the association between urinary levels of nine phthalate metabolites and the use of personal care products.

Subjects included 108 women who participated as controls in an ongoing population-based case-control study of environmental factors and genetic susceptibility to breast cancer in northern Mexico. Direct interviews were performed to inquire about sociodemographic characteristics, reproductive history, use of personal care products, and diet. Phthalate metabolites measured in urine by HPLC-MS/MS were monoethyl phthalate (MEP), monobenzyl phthalate (MBzP),

mono-n-butyl phthalate (MBP), mono-isobutyl phthalate (MiBP), mono-2-ethylhexyl phthalate (MEHP), mono-2-ethyl-5-oxohexyl phthalate (MEOHP), mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), mono-2-ethyl-5-carboxypentyl phthalate (MECCP), and mono-3-carboxypropyl phthalate (MCPP).

Detectable urinary concentrations of phthalate metabolites varied from 75% (MEHP) to 100% (MEP, MBP, MEOHP, MEHHP and MECPP). The use of anti-aging facial cream significantly increased the concentrations of MEP (β=0.83, 95%CI=0.13-1.53) and MCPP (β=0.5, 95%CI=0.04-0.97) respectively, whereas perfume use predicted increasing concentrations of MiBP (β=0.5, 95%CI=0.09-0.92) and, DEHP metabolites were significantly associated with deodorant (MEHP β= 0.59, 95%CI=0.18-1) and body lotion use (MECPP, β=0.47, 95%CI=0.08-0.85, MEHHP 0.49, 95% CI=0.08-0.87).

Our results suggest that the use of some personal care products contributes to phthalate body burden.

Key words: phthalates, personal care products, Mexican women

Introduction

Phthalate exposure in Mexico has been documented in regard to the use of plastic containers for foods and drinks (Bustamante-Montes 2007), plastic toys, feeding bottles, plastic training and drinking cups, pacifiers (Bustamante-Montes, Lizama-Soberanis et al. 2004), as well as medical devices (intravenous lines, blood bags and umbilical tubing) (Bustamante Montes, Garcia Fabila et al. 2005).

Personal care products, such as hair sprays, perfumes, deodorants and nail polishes may be a source of phthalate body exposure (Koo and Lee 2004). Diethyl phthalate (DEP), butylbenzyl phthalate (BBzP) and di(2-ethylhexyl) phthalate (DEHP), for instance, are used to manufacture perfume and fragrance products (Api 2001), hairspray (Houlihan, Brody et al. 2002), and nail polish and perfumes (Koo and Lee 2004), respectively. Additionally, the coatings of some medications were recently reported to contain dibutyl phthalate (DBP) (Hauser, Duty et al. 2004) and DEP (Hernandez-Diaz, Mitchell et al. 2009). Other products, such as construction materials (wallpaper, wire and cable insulation), car products (vinyl upholstery, car seats), clothing (footwear, raincoats), food packaging, children's products (Heudorf, Mersch-Sundermann et al. 2007), and medical devices such as intravenous solutions, blood, nutritional formulas and respiratory gases, are made with di(2-ethylhexyl) phthalate (DEHP) (Schettler 2006). Di-n-octyl phthalate (DOP), is also used to manufacture toys (Schettler 2006) ,flooring tiles, bottle cap liners, and as an indirect food additive (Heudorf, Mersch-Sundermann et al. 2007).

Routes of phthalate exposure include: inhalation of indoor and outdoor air (Wormuth, Scheringer et al. 2006; Hwang, Park et al. 2008; Garcia-Jares, Regueiro et al. 2009); ingestion of foods contaminated with phthalates by the leaching process from wrapping and plastic containers (Wormuth, Scheringer et al. 2006; Cao 2008); dermal contact through the use of personal care products (Duty, Ackerman et al. 2005; Frederiksen, Skakkebaek et al. 2007); and parenteral exposure from bags and/or tubing that deliver intravenous fluids, nutritional formulas and dialysis devices (Schettler 2006). Phthalates are metabolized in at least two phases, and low molecular weight phthalates are excreted in urine as monoester compounds, while the higher molecular weight phthalates undergo several biotransformations, including further hydroxylation and oxidation before they are excreted (Hauser and Calafat 2005).

Animal and human studies have shown that exposure to several phatalates impairs reproductive, respiratory health and development (Colon, Caro et al. 2000; Cobellis, Latini et al. 2003; Duty, Silva et al. 2003; Duty, Singh et al. 2003; Duty, Calafat et al. 2005; Hauser and Calafat 2005; Swan, Main et al. 2005; Reddy, Rozati et al. 2006; Hauser, Meeker et al. 2007; NRC 2008; Swan 2008; López-Carrillo, Hernández-Ramírez et al. 2009).

The objective of our study was to determine the association between the urinary concentrations of nine selected phthalate metabolites and the use of personal care products in Mexican women.

5. Materials and methods

Study population

As a part of an ongoing population-based case control study of the environmental and genetic factors of breast cancer in northern Mexico (López-Carrillo, Hernández-Ramírez et al. 2009), a cross-sectional study was performed including the first 108 controls that were recruited during January 2006 to December 2008. Eligible women were 19 years and older and permanently resided in the study area.

The Mexican sampling framework of national surveys (Tapia-Conyer et al. 1992) was used to identify controls. This tool included a list with 20 to 80 blocks in urban and rural areas to randomely locate households within the blocks. One elegible women was invited to participate per household, upon refusal the interviewer proceded to seek for another woman following the standardized guidelines that are reported elsewhere (López-Carrillo, Hernández-Ramírez et al. 2009).

Interviews and sample collection

Information about the use of personal care products (hair, face, hands and nails, feet and body products) in the last 48 hours was obtained by direct interviews. Also, women were queried about their socio-demographic, clinical, reproductive and dietary patterns among other characteristics. The same day of the interview the first urine sample of the morning was collected and kept frozen in a sterile plastic cup made of polypropylene and latex free (Medegen®) until further analysis. All women signed an informed participation consent form. The Ethics Committee of the National Institute of Public Health of Mexico approved this study.

Phthalate assessment

The measured metabolites were monoethyl phthalate (MEP), mono-*n*-butyl phthalate (MBP), mono-isobutyl phthalate (MiBP), monobenzyl phthalate (MBzP), mono(3-carboxypropyl) phthalate (MCPP), the hydrolytic mono(2-ethylhexyl) DEHP metabolite (MEHP) as well as the oxidative DEHP metabolites: mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), mono(2-ethyl-5-carboxypentyl) phthalate (MECPP). Determination of phthalate metabolites was made at the Organic Analytical Toxicology laboratories at CDC using solid phase extraction coupled with HPLC–MS/MS, according to the previously described methodology (Kato, Silva et al. 2005).

Statistical analyses

Selected sociodemographic characteristics and phthalate metabolite concentrations in the study population were assessed using descriptive and summary statistics. Concentrations of each metabolite below the LOD were imputed using the LOD value divided by square root of 2 (Finkelstein and Verma 2001). Urinary concentration of phthalates was adjusted for dilution dividing by creatinine concentration, following the methodology described elsewhere (Silva, Barr et al. 2004), and were normalized with a natural logarithm transformation. Two sample means comparison tests were performed to assess the difference between geometric means

reported on our study population and those reported in the NHANES (CDC 2005) for adult women.

Phthalate geometric means were compared according to the use of personal care products and consumption of bottled water by Student t-test. Simple linear regression models were used to assess the association between one or more personal care products use and phtahalate metabolite concentrations. The following covariates: age, BMI and years of scholarity were included in further analysis. All analyses were made using Intercooled STATA 9.2.

Results

The study population comprised mainly nonsmoking housewives with elementary education level (Table 1).

MEP, MBP and MECPP were detected in 100% of the samples while MEHP was detected in 75% (data not shown). Geometric means of MBP, MiBP, MCPP and most of DEHP metabolites, except MEHP, were higher compared to those reported by the NHANES for the U.S. female population aged 6 years and older ($p<0.05$), in contrast with MEP and MBzP, which were significantly lower in our study group (Table 2).

Several phthalate metabolite urine concentrations were significantly higher among users of the following personal care products compared with non users: body lotion (MEHHP, MEOHP and MECPP), deodorant (MEHP), perfume (MEP and MiBP), anti-aging facial cream (MEP, MBP,

MiBP and MCPP), eye shadow (MEP), hair conditioner (MBzP), hair styling products and shampoo (MEP) (Table 3).

Linear regression models showed the use of anti aging facial cream significantly predicted MEP, MBP and MCPP concentrations. Perfume use significantly increased MiBP concentration, Body lotion use was significantly related to MEHHP and MECPP while deodorante use to MEHP. Hair conditioner was associated with MBzP. Also bottle water consumption increased the DEHP metabolites (MEHHP, MEOHP) and MCPP (Table 4). These significant associations remained after adjusting by age, BMI and years of scholarity (socieconomical status proxy), except the coefficient for MBzP with hair conditioner that lost its significance (Data not shown).

A significant linear trend between the number of personal care products and the phthalates concentrations is shown in Figure 1.

Discussion

The results of this study show for the first time that in women residents of northern Mexico the use of certain personal care products is a source of exposure to DEP and probably to DEHP. Compared to non-users, women who reported the use of anti-aging facial cream, perfume and shampoo during 48 hours previous to the interview showed significantly higher urinary concentration of MEP (the main DEP metabolite). On the other hand, the use of deodorant was associated to a significant increase in urinary levels of MEHP (a DEHP metabolite). The combined use of more than two personal care products in addition to shampoo (*i.e.*, perfume,

anti-aging facial cream, hair care products and/or eye shadow) during 48 hours previous to the urine sampling significantly increased urinary MEP concentrations. Additionally, bottled-water consumption was associated to an increase in the levels of MEHHP and MEOHP, also DEHP metabolites.

These results are consistent with most previous studies carried out in other countries, which report the use of personal care products as a potential source of phthalate exposure (DiGangi, Harm et al. 2002; DiGangi, Schettler et al. 2002; Houlihan, Brody et al. 2002; CIR 2003; Koo and Lee 2004; Chingin, Chen et al. 2009) not only in women (Koo and Lee 2004; Berman, Hochner-Celnikier et al. 2009) but also in men (use of cologne and after shave cream) (Duty, Ackerman et al. 2005) and in babies (use of lotion, powder and shampoo) (Sathyanarayana, Karr et al. 2008), contrasting only with a study carried out in men (Duty, Ackerman et al. 2005), in which the use of lotion was associated to a significant decrease in urinary MEHP levels, without any clear explanation by the authors.

Correspondingly, our results are consistent with an increase in urinary phthalate concentrations with an increased number of products used, as has been reported in other studies in men (Duty, Ackerman et al. 2005), babies (Sathyanarayana, Karr et al. 2008), as well as in pregnant women (Berman, Hochner-Celnikier et al. 2009), those of whom reported combined use of four or more products (perfume, deodorant, lipstick, nail polish and/or hand or face cream) showed up to 4 times higher average MEP concentrations than women who used less than four products (Berman, Hochner-Celnikier et al. 2009).

Furthermore, the relationship found by our study between bottled-water consumption and DEHP metabolites MEHHP and MEOHP is similar to the findings reported by other studies (Montuori, Jover et al. 2008), since DEHP diffusion from plastic bottles into water has been documented (Cao 2008; Wagner and Oehlmann 2009).

Urinary concentrations of various phthalates vary across the world (Koch, Rossbach et al. 2003; CDC 2005; Huang, Kuo et al. 2007; Adibi, Whyatt et al. 2008; Berman, Hochner-Celnikier et al. 2009; Peck, Sweeney et al. 2009). As for the results reported by NHANES, average MBP, MiBP, MEHHP and MEOHP concentrations in the general population of the United States (CDC 2005) were shown to be significantly lower than those observed in our study (MBP=21.7 vs. 72.43, MiBP=2.87 vs. 8.36, MEEHHP=19.7 vs. 45.84, MEOHP=13.5 μg/g 31.81 μg/g creatinine). On the other hand, the median of MEP in our study was 55.9 μg/L, lower than that observed in (African American and Domincan) women residents of New York City and in (Arab and Israeli) women in Jerusalem, which were 202 and 165 μg/L, respectively (Adibi, Whyatt et al. 2008; Berman, Hochner-Celnikier et al. 2009). As for DEHP metabolites, the median of MEHP in our study was 3.8 μg/L, lower than that observed in Asiatic women: 20.6 μg/L in Taiwanese women (Huang, Kuo et al. 2007), and 4.5 μg/L in women migrants from Laos residing in the US (Peck, Sweeney et al. 2009). Contrariwise, MEHHP and MEOHP means were higher in the women in our study (34.5 μg/L and 22.1 μg/L, respectively) than in women in Jerusalem (MEHHP= 21.5 and MEOHP=17.5 μg/L), US residents (MEHHP= 18.2 μg/L, and in New York City MEOHP=17.5 μg/L) (CDC 2005; Adibi, Whyatt et al. 2008). As for MCPP (a DOP metabolite), the respective means in various studies are similar (about 3 μg/L) (CDC 2005; Adibi, Whyatt et al. 2008; Berman, Hochner-Celnikier et al. 2009; Peck, Sweeney et al. 2009).

Although these differences can be due to variations in use patterns, as well as to phthalate concentrations in personal care products worldwide, they might be a result of variations in the individual genetic susceptibility to metabolize phthalates.

The interpretation of our results includes certain methodological considerations. Identification of phthalate exposure sources in this study is not comprehensive. On one hand, there are other sources –such as intake through foods (Schettler 2006); building materials (vinyl floors and wall paper) (Hauser and Calafat 2005), and the use of medical treatments (blood transfusions and administration of IV solutions) (Schettler 2006) – that were not explored. On the other, certain phthalates potentially present in various personal care products were not identified in this study population in relation to their use. Particularly, concentrations of the main DBP metabolite (MBP) – which is used for making nail polish (67%) (Houlihan, Brody et al. 2002), deodorants, perfumes (DiGangi, Harm et al. 2002; Houlihan, Brody et al. 2002), in hair spray and styling mousse (DiGangi, Harm et al. 2002)–, and of DOP (whose main metabolite is MCPP) –which is used for making certain deodorants (21%) (DiGangi, Harm et al. 2002), were not associated with the use of those products, with the exception of anti-aging facial cream. On one hand, it seems possible that there may be substantial differences in the formulation of personal care products used in Mexico that could explain the above situation, but this study does not provide such information. On the other, the lack of statistical power may have limited the detection of associations between the various phthalates (especially the less frequent metabolites) and the use of infrequently utilized personal care products by this population.

As for DEHP, our results showed an association between the use of deodorants and MEHP, but not oxidative metabolites (MEHHP, MEOHP, and MECPP), which together represent a larger exposure ratio, compared to MEHP (according to evidence on oral exposure of 61.5 vs. 7.3%) (Silva, Reidy et al. 2006); therefore we cannot rule out a spurious association due to multiple comparisons. In turn, the use of body lotion was significantly associated to MEHHP and MECCP, but insignificantly to MEHP; this might be a result of the lack of statistical power, which also limited the possibility of analyzing the metabolites by product brands and types.

On the other hand, since phthalate metabolism occurs within time periods of 2 to 48 hours (Wittassek and Angerer 2008), and phthalates do not accumulate in the body, exposure measurement based on a single spot urine sample might not reflect a chronic exposure, even though, according to several reports, the use of personal care products is relatively consistent (Loretz, Api et al. 2005; Loretz, Api et al. 2006; Loretz, Api et al. 2008), thus a single measurement may be a good estimate of chronic exposure (Engel, Zhu et al. 2009). This is supported by several studies suggesting that, though there may be some variability in time, it is possible to use a single spot urine sample to estimate exposure up to one year in children (Teitelbaum, Britton et al. 2007), three months in men (Hauser, Meeker et al. 2004), and a month in women (Peck, Sweeney et al. 2009).

As for the validity of the exposure assessment, the selected metabolites match only the respective parent compounds: DEP (MEP), BBzP (MBzP), DBP (MBP, MCPP), DiBP (MiBP), DEHP (MEHP, MEOHP, MEHHP, MECCP) and DOP (MCPP) (Barr, Silva et al. 2003; Calafat, Silva et al. 2006; Koch, Preuss et al. 2006; Silva, Reidy et al. 2006; Koch and Calafat 2009), which

reduces sample pollution due to father compound ubiquity (Barr, Silva et al. 2003) and increases measure especificity. Besides, they may be regarded as sensitive biomarkers, since MEP, for instance, represents up to 70% of the absorbed DEP dose (Frederiksen, Skakkebaek et al. 2007).

Phthalate exposure is an emerging environmental health concern that warrants attention due to their potential health impact as it has been recently suggested with breast cancer (López-Carrillo, Hernández-Ramírez et al. 2009).

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Tables and figures

Table 1. Sociodemographic characteristics of the study women

Characteristic	Mean (Range)	n (%)
Age		
Years	53.5 (32 - 79)	
BMI		
Kg/m^2	28.6 (17.3 - 53.4)	
Smoking		
Yes		15 (13.9)
No		93 (86.1)
Education level		
None		7 (6.5)
Elementary		73 (67.6)
Secondary		20 (18.5)
High school and up		8 (7.4)
Occupation		
Home		93 (86.1)
Remunerated occupation		15 (13.9)

Table 2. Phthalate concentrations (Geometric means) in this study vs. USA NHANES

Metabolites (μg/g creatinine)	Subjects (n=108) GM (95% CI)	NHANES* (n=1411) GM (95% CI)
MEP**	83.2 (67.3 - 102.9)	187 (166-210)
MBP**	72.4 (59.9 - 87.6)	21.7 (19.6-23.9)
MiBP**	8.4 (7.1 - 9.8)	2.9 (2.6-3.2)
MBzP**	4.4 (3.5 - 5.5)	15.7 (14.2-17.3)
DEHP metabolites		
MEHP	5.2 (4.3 - 6.2)	4.5(4-5.1)
MEHHP**	45.8 (39.6 - 53.1)	19.7(17.3-22.5)

MEOHP**	31.8 (27.6 - 36.6)	13.5(11.9-15.3)
MECPP	71.9 (62.6 - 82.5)	-
MCPP**	3.9 (3.4 - 4.5)	2.8(2.5-3.2)

*Women only, 6 years and older (CDC 2005) **($p<0.05$)

Table 3. Phthalate concentrations (Geometric means/ μg/g creatinine) according to source of exposure

Source of exposure	MEP	MBP	MiBP	MBzP	MEHP	MEHHP	MEOHP	MECPP	MCPP
Personal care products									
Body lotion									
No (n=16)	71.2	110.6*	8.7	5.8	5	29.5	22.6	48.3	4.9
Yes (n=92)	85.5	67.3	8.3	4.2	5.2	49.5*	33.8*	77*	3.8
Deodorant									
No (n=27)	71.6	70.1	9.3	4.9	3.3	38.3	26.3	60.5	3.7
Yes (n=81)	87.5	73.2	8.1	4.2	6*	48.7	33.9	76.1	4
Perfume									
No (n=89)	75.1	68	7.6	4.2	5.1	45.6	31.7	71.7	3.8
Yes (n=19)	134.3*	97.7	12.6*	5.3	5.3	47.1	32.5	72.6	4.4
Anti-aging facial cream									
No (n=97)	76.5	64.2	7.9	4.5	5.1	45.9	32.2	72.3	3.7
Yes (n=11)	175.3*	209*	13.3*	3.6	6.1	45	28.8	68.1	6.5*
Eye shadow									
No (n=103)	78.7	72.3	8.1	4.4	5.1	45.6	31.7	71.5	3.9
Yes (n=5)	258.7*	74.9	14.1	4.3	6.8	51.7	35	80.6	3.7
Hair conditioner									
No (n=72)	75.9	75.3	7.6	3.7	4.8	44.5	30.6	68.7	4.2
Yes (n=36)	99.9	67	10.1	6.2*	6	48.6	34.4	78.6	3.5
Gel, spray or mousse									
No (n=99)	77.9	72.6	8.4	4.3	5.1	47.2	32.8	73.2	4
Yes (n=9)	172.4*	70.9	8	5.5	5.4	33.1	23.1	59	3.4
Shampoo									
No (n=15)	49.2	76.7	8.8	3.7	3.8	38.6	27.9	66	3.4
Yes (n=93)	90.6*	71.8	8.3	4.5	5.4	47.1	32.5	72.9	4
Plastic									

Containers									
Bottled water									
No (n=44)	89.8	60.1	8.2	4.4	5.3	35.7	24.7	57.6	3.1
Yes (n=64)	78.9	82.4	8.4	4.4	5.1	54.5*	37.8*	83.6*	4.6*
Food containers									
No (n=62)	68.1	70.2	7.7	4.4	4.5	45.5	32.3	68	4.1
Yes (n=46)	108.9*	75.6	9.4	4.4	6.2	46.3	31.2	77.4	3.7

*p < 0.05

Table 4. Linear regression coefficients for urinary phthalate concentrations and personal care product use (yes/no)

Metabolites (µg/g)	**Body lotion**	**Deodorant**	**Perfume**	**Anti-aging facial cream**	**Hair conditioner**	**Bottled water**
MEP						
β				0.83*		
(95% CI)				(0.13-1.53)		
MBP						
β				1.18*		
(95% CI)				(0.58-1.78)		
MiBP						
β			0.5*			
(95% CI)			(0.09-0.92)			
MBzP						
β					0.54*	
(95% CI)					(0.05-1.02)	
MEHP						
β		0.59*				
(95% CI)		(0.18-1)				
MEHHP						
β	0.47*					0.4*
(95% CI)	(0.08-0.87)					(0.11-0.68)
MEOHP						
β						0.42*
(95% CI)						(0.14-0.7)
MECPP						
β	0.47*					
(95% CI)	(0.08-0.85)					
MCPP						
β				0.5*		0.39*
(95% CI)				(0.04-0.97)		(0.1-0.67)

*p<0.05

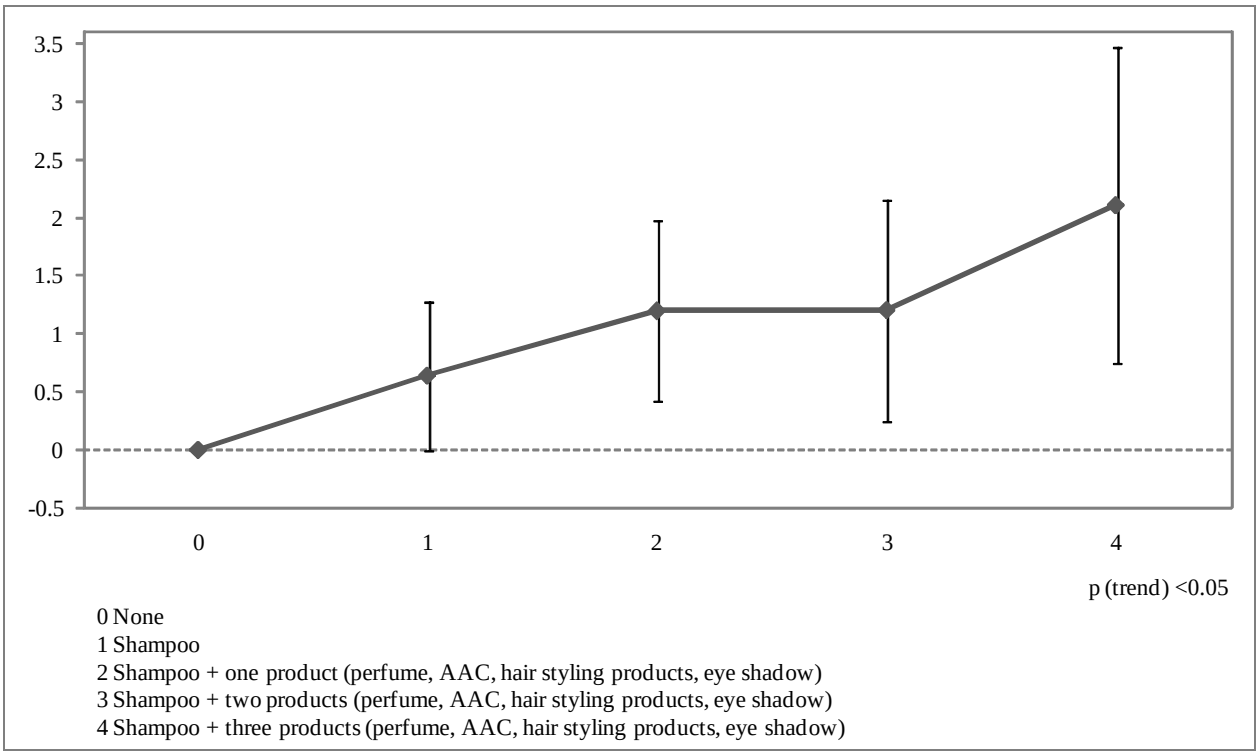

Figure1. Regression coefficients of phthalate metabolite concentrations according to increasing number of products used.