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RESEARCH ARTICLE

Blood concentrations and risk assessment of persistent organochlorine compounds in newborn boys in Turkey. A pilot study

Onur Kenan Ulutaş[1] · İsmet Çok[1] · Feyza Darendeliler[2] · Banu Aydin[2] · Asuman Çoban[2] · Bernhard Henkelmann[3] · Karl-Werner Schramm[3,4]

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Abstract Even early life in utero cannot provide a safe place for newborns. The first acquaintance with chemicals takes place in utero and/or with mother's milk after delivery. Besides legislations and bans to persistent organic pollutants (POPs), these chemicals are still affecting the general population especially the children as they are one of the populations most susceptible to chemicals, and also the health problems may arise in the future. Our objective is to collect the first data in newborns in Turkey to determine baseline levels of POPs in the general population and estimate the potential cancer risk related to exposure. Twenty-nine organochlorine pesticides (OCPs) and 18 polychlorinated biphenyl (PCB) congeners in blood samples of newborn boys (0–1 month old) who were born in İstanbul, Turkey, in 2010–2012 were evaluated with high-resolution gas chromatography–high-resolution mass spectrometry (HRGC/HRMS). Results for analyzed chlorinated compounds are as follows: hexachlorocyclohexane (ΣHCH) 1828±3650 pg/g lipid, dichlorodiphenyltrichloroethane (ΣDDT) 10,000±15,398 pg/g lipid, and ΣPCB 1068±1823 pg/g lipid. 4,4′-DDT, 4,4′-dichlorodiphenyldichloroethylene (4,4′-DDE), hexachlorobenzene, and PCB 138 and 153 are the major contaminants. New POPs as lindane 61±268 pg/g lipid, pentachlorobenzene 13±74 pg/g lipid, and endosulfan 29±106 pg/g lipid are also detected in blood. Estimated total risk for lifetime PCB exposure is less than 1×10^{-5}, an acceptable risk. Blood concentration levels will be important base data in the assessment of health concerns of newborns as well as for studies about how endocrine disruptors affect humans.

Keywords OCP · PCB · Blood · Newborn · Boy · Turkey

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✉ Onur Kenan Ulutaş
onurkenan@gmail.com

[1] Department of Toxicology, Faculty of Pharmacy, Gazi University, Yenimahalle, 06330 Ankara, Turkey

[2] Department of Pediatrics, İstanbul Medical Faculty, İstanbul University, İstanbul, Turkey

[3] Molecular Exposomics, Helmholtz Zentrum München – Deutsches Forschungszentrum für Gesundheit und Umwelt, Ingolstädter Landstr 1, 85764 Neuherberg, Germany

[4] Wissenschaftszentrum Weihenstephan für Ernährung, Landnutzung und Umwelt, Department für Biowissenschaften, Technische Universität München, Weihenstephaner Steig 23, 85350 Freising, Germany

Introduction

Child health is the basis of adult health. Particularly noteworthy is that adult disorders may have a fetal origin, although onset of the clinical problem may not be noted until the reproductive age has been reached (WHO 2012). Animal experiments have clearly demonstrated that there are sensitive developmental periods when chemicals of concern cause permanent organizational changes that may appear as structural and functional anomalies much later. Even more, adverse prenatal environments can promote metabolic disease in offspring and subsequent generations (Radford et al. 2014). Fetal development is a critical period for all these disorders. Although these trends are established, our understanding of their causes is quite poor (WHO 2012, 2013).

Prenatal life is the most sensitive stage of human development to environmental pollutants. Early exposure to chemicals such as persistent organic pollutants (POPs) may increase the risk of adverse health effects especially during childhood (Main et al. 2007; Darnerud et al. 2010; Radford et al. 2014). Since the testicular germ cell cancers, congenital

cryptorchidism, hypospadias, and semen quality factors are suspected to be caused, at least partially, by exposure to some POPs during early life, male reproductive health and prenatal/postnatal life has become a major focus of POP research (Pierik et al. 2004; Damgaard et al. 2006; Main et al. 2007; Govarts et al. 2012; Kezios et al. 2013). Exposure to contaminants was suggested as a risk factor, and all disease could be a related component of single underlying condition, which is demonstrated as testicular dysgenesis syndrome (TDS) (Skakkebaek 2004; Skakkebæk et al. 2007). The concept of TDS is based on the idea that the associated symptoms have a common origin in fetal development, and the extent and severity of the symptoms are dependent on the degree to which normal developmental processes have been troubled. In addition, it assumes that any distress is because of the POP exposure or other possible factors while the male programming window is irreversible and have lifelong implications for the affected individual and, potentially, also for their offspring (Skakkebaek et al. 2007).

Even more, intrauterine chemical exposures can be dramatically more harmful than exposures in life. Substantial scientific evidence demonstrates that children face amplified risks from their body burden of pollution. Vulnerability derives from both rapid development and incomplete defense system such as immature barrier systems and low level of chemical binding proteins which allow chemicals to reach target organs even with higher concentrations (Eskenazi et al. 1999; Grandjean et al. 2008). Moreover, birth outcomes may be intermediate between prenatal toxic exposures and various health outcomes in later life; hence, the in utero effects of environmental agents on pregnancy outcomes are of interest.

The potential adverse effects of environmental chemicals on children's health and development are a matter of widespread public health concern. Especially organochlorine pesticides (OCPs) and polychlorinated biphenyls (PCBs) constitute the most striking ones. Maternal serum and cord blood levels of dichlorodiphenyltrichloroethane (DDT) and/or dichlorodiphenyldichloroethylene (DDE) have been associated in some studies with preterm birth (Longnecker et al. 2001; Ribas-Fito et al. 2002), reduced birth weight (Al-Saleh et al. 2012; Kezios et al. 2013), and head circumference (Wolff et al. 2007). Several studies of low-level PCB exposure during pregnancy also reported associations with decreased birth weight or other birth outcomes (Govarts et al. 2012; Kezios et al. 2012; Murphy et al. 2010); other studies found no convincing evidence of these associations (Gladen et al. 2003; Givens et al. 2007; Wolff et al. 2007). A few studies have examined the effects of other organochlorine pesticide exposure, such as HCB, with inconsistent findings in relation to birth outcomes (Gladen et al. 2003; Brucker-Davis et al. 2010).

The Stockholm Convention on persistent organic pollutants (2008) recommends to determine baseline exposures to POP in the general population; however, exposure to these chemicals may still be an issue of concern and can still be affecting especially the more susceptible ones such as newborns and children. Even more, not only in Turkey but also in the world, the information about newborn exposure to POPs is very limited. The aim of this study was not only to determine the levels of OCPs and PCBs in blood samples of newborns but also to estimate cancer risk starting the very first days of life which will supply noteworthy data to healthy generations.

Materials and methods

Subjects

Between 2010 and 2012, whole blood samples (1–3 mL) were taken from 37 healthy newborn boys whose mothers were living in Istanbul, Turkey. Blood samples were provided by the Department of Pediatric Endocrinology and Neonatology, Faculty of Medicine, İstanbul University. All obtained blood samples were mixed with heparin and stored in glass containers at −20 °C until analysis. The age of subjects ranged from 0 to 1 month. All families acknowledged their participation by signing an informed consent form. All participant mothers completed a detailed questionnaire about age, possible exposure through occupational contact, dietary habits, smoking habits, and other data. All mothers were mixed food consumers and had no occupational history to OCP and PCB exposures. The study protocol was reviewed and approved by the Ethics Committee of Istanbul University for Human Studies of the School of Medicine, Istanbul (ethics committee number: 27.08.2009-2466).

Chemicals and analytical methods

All solvents used were of trace analysis quality. Concentrations of all investigated OCPs and PCBs were determined by the isotope dilution method, which provides highly accurate and reliable data for international comparisons. Samples were spiked with ^{13}C-labeled 960 μL PCB and 310 μL OCP internal standards before extraction and with ^{13}C-labeled recovery standards before high-resolution gas chromatography–high-resolution mass spectrometry (HRGC-HRMS) analysis. The ^{13}C-labeled OCP recoveries averaged 50–150 % and the ^{13}C-labeled PCB recoveries averaged 80–110 %. One procedure blank consisting of purified water and one lab reference solvent blank were analyzed for every ~10 samples analyzed. The sample results were corrected by blank values if detected. For that, the mean of all blanks analyzed and the corresponding standard deviation was calculated. Then, the sample results were subtracted by its blanks. The residue was required to be greater than three times the standard deviation, which is defined as the limit of detection (LOD); otherwise, the result is expressed as not

detectable. In the case where no blank values were detected for an analyte, the LOD was calculated as three times the signal noise of the related mass trace registered by the MS.

Chemical extraction and cleanup

After sequential adding of the ^{13}C-labeled OCPs and PCBs, 2.5 mL saturated potassium oxalate solution, 5 mL ethanol, 5 mL diethyl ether, 5 mL n-pentane, and the human blood sample were liquid–liquid-extracted. The aqueous phase was again extracted two times with 5 mL of n-pentane. The combined organic phases were dried over anhydrous sodium sulfate and evaporated for gravimetrical determination of the lipid content. The lipid contents of samples ranged from 0.02 to 0.44 g individually and mean lipid content % of blood samples was 4.84 %. The lipid was dissolved again with approximately 1–2 mL mixture of n-hexane/dichlomethane (1:1) and the samples underwent cleanup using a mixed column (10 g silica, 5 g alumina with 3 % H_2O, and 2 g anhydrous sodium sulfate). The extracts were eluted with 100 mL of a mixture of n-hexane and dichloromethane (1:1) and reduced to 1 mL. The residues were further purified through a C18 SPE cartridge for which acetonitrile was used as the eluting solvent. After adding a recovery standard, the extracts were concentrated with a gentle flow of nitrogen to 20 μL as preparation for analytical determination.

Instrumentations

The analytical methods and quality control procedures for blood analyses were laid out by the Institute of Ecological Chemistry, Helmholtz Zentrum München, German Research Center for Environmental Health, Germany. The OCP and PCB analyses were performed with a high-resolution mass spectrometer Finnigan MAT 95S (Thermo Electron GmbH, Bremen, Germany) coupled with an Agilent GC 6890 (Agilent Technologies, Palo Alto, CA, USA). Chromatographic separation was achieved by 0.5 μL for OCP and 0.8 μL for PCB splitless injection (cold injection system CIS4, Gerstel GmbH, Mulheim, Germany) on a ZB-MultiResidue2 column with a length of 30 m, ID 0.25 mm, and 0.2-μm film length (Phenomenex). The GC oven was programmed as follows: for OCPs, 80 °C initial hold for 1.5 min, increase at a rate of 10 °C/min to 320 °C, and a final hold for 15 min; and for PCBs, 90 °C initial hold for 1.5 min, increase at a rate of 20 °C/min to 170 °C, hold for 7 min, followed by an increase of 3.5 °C/min to 265 °C, followed by an increase of 20 °C/min to 310 °C, and a final hold at 310 °C for 10 min. The mass spectrometer was operated in SIM mode at a resolution of >8000, and the two most intense ions of the molecular ion or an abundant fragment ion cluster were monitored for the unlabeled and labeled isomers.

Statistical analyses

Lipid adjusted concentrations were used in the analysis, as they provide a better estimate of the body burden. The values of below LOD were assigned as zero to calculate the total concentrations of chemicals. All values given were calculated by SPSS software version 13.0 for Windows (SPSS Inc., Chicago, IL, USA). Values in the text are medians or means ±standard deviation (SD).

Results

The blood OCP and PCB concentrations found in this study are summarized in Table 1. All chemicals that were evaluated except PCB 81, PCB 126, PCB 169, heptachlor, and trans-heptachlor epoxide were detected in the studied group. 4,4′-DDT (290±861 pg/g lipid), 4,4′-DDE (9299±14,388 pg/g lipid), and hexachlorobenzene (977±2949 pg/g lipid) were the major contaminants, as they have the highest concentrations and are the most common contaminants in the studied blood samples. β-Hexachlorocyclohexane (β-HCH) is the dominant contaminant in the hexachlorocyclohexane group, and the detected mean concentration was 1445.1±2135 pg/g lipid. New members of POPs—lindane, pentachlorobenzene, and endosulfan—were analyzed, and mean concentrations in blood samples were 61±268, 13±74, and 29±106 pg/g lipid, respectively. The most common DDT congener was 4,4′-DDE which was detected over 80 % of the newborns with the mean concentration of 9299±14,388 pg/g lipid. New exposure to DDT seems to be very low as detection rate for 4,4′-DDT was 21 % and concentration was $^1/_3$2 that of 4,4′-DDE with 290.19±861.03 pg/g lipid in newborn bloods. Results for analyzed main chlorinated compounds were ∑DDT 10,000±15,398 pg/g lipid and ∑HCH 1828±3650 pg/g lipid, respectively.

Detection rate of the pesticides such as aldrin, dieldrin, endrin, endosulfan, methoxychlor, and mirex was distributed in a range of 2–21 % of the newborns. Dieldrin's concentration was 80.43±241.57 pg/g lipid while aldrin's and endrin's concentrations were very low. Hexachlorobenzene mean concentration was 977.39±2949.47 pg/g lipid and detected in 50 % of the participants. On the other hand, pentachlorobenzene, pentachloroanisol, and octachlorostyrene were detected in less than 10 % of the boys. Concentration of oxy-chlordane was 39.33±61.71 pg/g lipid with a detection rate of 37 %. Cis-chlordane and trans-chlordane were detected of concentrations 21.35±93.94 and 22.49±67.04, respectively.

PCB congeners were present in 62 % of all blood samples and calculated as ∑PCB 1068±1823 pg/g lipid in the current study. PCB 138 and 153 were only detected as 27 % of the participants to the study. Other indicator PCB congeners PCB 28, 52, 101, and 180 were detected in 5–13 % of the group.

Table 1 Concentrations of OCPs and PCBs in blood of newborn boys (pg/g lipid)

Compound	*n*	*N* (*N*%)	Median	Mean	±SD	Min	Max
α-HCH	37	4 (10.8)	<LOD	19.66	87.77	<LOD	530.33
β-HCH	37	30 (81.1)	947.38	1445.1	2135.83	<LOD	10,255.19
γ-HCH	37	2 (5.4)	<LOD	61.93	268.07	<LOD	1309.62
δ-HCH	37	2 (5.4)	<LOD	0.46	2.05	<LOD	11.10
ε-HCH	37	3 (8.1)	<LOD	301.52	1684.55	<LOD	10,367.78
Total HCH	37	31 (83.8)	996.91	1828.68	3650.59	<LOD	21,153.3
4,4′-DDT	37	8 (21.6)	<LOD	290.19	861.03	<LOD	4016.01
2,4′-DDT	37	9 (24.3)	<LOD	92.45	315.94	<LOD	1875.50
4,4′-DDD	37	6 (16.2)	<LOD	174.14	534.59	<LOD	2757.24
2,4′-DDD	37	7 (18.9)	<LOD	131.73	393.92	<LOD	1863.94
4,4′-DDE	37	30 (81.1)	5207.9	9299.23	14,388.7	<LOD	81,644.4
2,4′-DDE	37	6 (16.2)	<LOD	12.65	37.92	<LOD	205.52
Total DDT	37	30 (81.1)	5420.31	10,000.4	15,398.8	<LOD	87,515.6
Pentachlorobenzene	37	4 (10.8)	<LOD	13.72	74.53	<LOD	459.75
Hexachlorobenzene	37	18 (48.6)	<LOD	977.39	2949.47	<LOD	17,681.7
Pentachloroanisole	37	2 (5.4)	<LOD	15.55	87.41	<LOD	537.67
Octachlorostyrene	37	3 (8.1)	<LOD	7.59	28.55	<LOD	142.35
trans-Chlordane	37	7 (18.9)	<LOD	22.49	67.04	<LOD	284.67
cis-Chlordane	37	2 (5.4)	<LOD	21.35	93.94	<LOD	491.07
oxy-Chlordane	37	14 (37.8)	<LOD	39.33	61.71	<LOD	222.60
Heptachlor	37	0 (0)	<LOD	<LOD		<LOD	<LOD
cis-Heptachloroepoxide	37	12 (32.4)	<LOD	55.38	148.07	<LOD	823.38
trans-Heptachloroepoxide	37	0 (0)	<LOD	<LOD		<LOD	<LOD
Aldrin	37	1 (2.7)	<LOD	1.67	10.32	<LOD	63.65
Dieldrin	37	8 (21.6)	<LOD	80.43	241.57	<LOD	1319.93
Endrin	37	1 (2.7)	<LOD	0.92	5.72	<LOD	35.26
Endosulfan-I	37	6 (16.2)	<LOD	29.35	106.08	<LOD	630.93
Endosulfan-II	37	2 (5.4)	<LOD	1.33	6.00	<LOD	32,8
Methoxychlor	37	7 (18.9)	<LOD	40.04	108.92	<LOD	536.73
Mirex	37	3 (8.1)	<LOD	46.63	257.79	<LOD	1588.41
PCB #28	37	5 (13.5)	<LOD	37.96	115.38	<LOD	553.46
PCB #52	37	3 (8.1)	<LOD	148.35	713.43	<LOD	4274.44
PCB #101	37	2 (5.4)	<LOD	53.19	259.16	<LOD	1525.29
PCB #138	37	10 (27.0)	<LOD	223.26	440.41	<LOD	1460.08
PCB #153	37	10 (27.0)	<LOD	191.43	443.42	<LOD	1768.29
PCB #180	37	3 (8.1)	<LOD	37.69	149.97	<LOD	797.39
total indicator PCB	37	14 (37.8)	<LOD	691.91	1365.22	<LOD	5685.15
PCB #77	37	5 (13.5)	<LOD	11.66	42.75	<LOD	222.15
PCB #81	37	0 (0)	<LOD	<LOD		<LOD	<LOD
PCB #126	37	0 (0)	<LOD	<LOD		<LOD	<LOD
PCB #169	37	0 (0)	<LOD	<LOD		<LOD	<LOD
Total non-ortho-PCB	37	5 (13.5)	<LOD	11.66	42.75	<LOD	222.15
$\sum WHO_{non\text{-}ortho\text{-}PCB}$-TEQ				0.001166			
PCB #105	37	3 (8.1)	<LOD	27.79	102.51	<LOD	519.28
PCB #114	37	10 (27.0)	<LOD	13.41	30.26	<LOD	125.95
PCB #118	37	5 (13.5)	<LOD	37.78	125.62	<LOD	543.88
PCB #123	37	1 (2.7)	<LOD	39.23	238.64	<LOD	1451.61
PCB #156	37	8 (21.6)	<LOD	26.36	69.40	<LOD	279.06
PCB #157	37	9 (24.3)	<LOD	19.43	42.42	<LOD	157.04

Table 1 (continued)

Compound	*n*	*N* (*N*%)	Median	Mean	±SD	Min	Max
PCB #167	37	6 (16.2)	<LOD	10.58	39.99	<LOD	233.65
PCB #189	37	2 (5.4)	<LOD	2.16	10.60	<LOD	62.47
Total mono-ortho-PCB	37	20 (54.1)	25.73	176.77	372.46	<LOD	1775.73
$\sum WHO_{mono\text{-}ortho\text{-}PCB}$-TEQ				0.005303			
Total PCB	37	23 (62.2)	214.28	1068.79	1823.66	<LOD	6006.11
$\sum WHO_{PCB}$-TEQ				0.00647			

*F*or mean and average values, the values of below LOD were assigned as zero.

n number of newborns participated into the study, *N* number of samples with concentration above LOD, *N%* percentage of the samples with concentration above LOD, *LOD* limit of detection

For non-ortho-PCB congeners, only PCB 77 was detected in 13 % of the newborns. Other non-ortho-congeners PCB 81, 126, and 169 were not detected in none of the blood samples. $WHO_{non\text{-}ortho\text{-}PCB}$-toxicity equivalence (TEQ) value was 0.00116. Maximum % detected mono-ortho-PCB congener was PCB 114. PCB 114 was detected in 27 % of the blood samples with 13.41±30.26 pg/g lipid concentration. PCB 156 concentration was 26.36±69.40 pg/g lipid and that of PCB 157 was 19.43±42.42 pg/g lipid, both were detected in only 21 % of the newborns. Other mono-ortho-group PCB congener's availability rates were between 16 and 2 %. $WHO_{mono\text{-}ortho\text{-}PCB}$-TEQ and total $WHO_{\Sigma PCB}$-TEQ values were 0.0053 and 0.0064, respectively.

Discussion

Human exposure to persistent organic pollutants (POPs) begins in the uterine life period by trans-placental transfer, and placenta may prevent transfer of some pollutants, but there is evidence that POPs, even those of high molecular weight, can reach the fetuses (Vizcaino et al. 2011, 2014). Transfer of contaminants during pregnancy may have implications for fetus health. Placenta cannot even block all chemicals at all, and as most of these chemicals are lipophilic in structure, intrauterine exposure is inevitable. Mothers of these newborns were living in Istanbul, Turkey. It is a highly industrialized region of Turkey and PCB exposure may be high. While Istanbul does not host any agricultural areas and OCP usage and exposure can be expected to be low, most OCPs are widely distributed geographically; therefore, exposure is unavoidable. In utero exposure may lead to severe outcomes for newborns and may predispose to late adult deleterious effects (Boekelheide et al. 2012). Thus, in utero exposure to POPs such as PCBs and OCPs has shown to increase the risk of adverse development outcomes in children (Ribas-Fito et al. 2007; Park et al. 2008; Valvi et al. 2012). These results have increased notably the interest of the scientific community on exposure to these compounds during gestation. However, some studies could not demonstrate the same results, as increased levels of DDT and/or DDE in maternal serum, cord blood, or breast milk were not related to adverse birth outcomes (Fenster et al. 2006; Pathak et al. 2009; Garced et al. 2012; Govarts et al. 2012).

PCB and OCP levels in cord blood vary substantially between countries and geographical areas (Table 2). Vizcaino et al. (2014) show that 4,4′-DDE median levels are 175 ng/g in cord serum obtained from mother/newborns in Spain, although Fukata et al. (2005) determined only 2.8 ng/g cord serum level in a Japanese population. The levels found in Sweden (95 ng/g) are 54 % higher than those in Spain (Darnerud et al. 2010). HCB levels are also higher in Spain (49.5 ng/g) than the levels in Belgium, 22.6 ng/g, and Italy,

Table 2 The median OCP and PCB concentrations in cord blood samples of different countries (ng/g lipid)

Country, year	Reference	*n*	4,4′-DDE	4,4′-DDT	β-HCH	HCB	PCB 118	PCB 138	PCB 153	PCB 180	ΣPCB
Sweden 1996–1999	Darnerud et al. 2010	160	95	–	–	–	–	–	–	–	139
Japan 2002–2003	Fukata et al. 2005	20	2.8	–	2.8	1.1					63
Belgium 2002–2003	Sioen et al. 2013	270	124.0	–	–	22.6	–	–	–	–	74.5
Slovakia 2002–2004	Patayova et al. 2013	1134	393.348	17.427	8.61	73.989	0.018	0.187	0.269	0.213	–
Spain 2004–2008	Vizcaino et al. 2014	308	175	33.3	16.9	49.5	<LOD	32.2	47.1	27.8	–
Italy 2006	Bergonzi et al. 2009	70	112.3	–	–	19.4	–	–	–	–	198.2

ΣPCB: Sum of PCB 138, 153, and 180

LOD limit of detection

19.4 ng/g (Sioen et al. 2013; Bergonzi et al. 2009). Patayová et al. (2013)) have demonstrated the highest 4,4′-DDE levels in the Europe zone with 393.348 ng/g lipid. Although 4,4′-DDT exposure seemed to be lower than in Spain, the determined value was 17.427 ng/g lipid. HCB levels were also the highest with 73.989 ng/g lipid median value, but PCB exposure seemed to be very low (PCB 118 0.018 ng/g lipid, PCB 138 0.187 ng/g lipid, PCB 153 0.269 ng/g lipid, PCB 180 0.213 ng/g lipid).

During the prenatal period, the developing body is particularly sensitive from exposure to chemicals compared to during postnatal period, making it crucial to assess the exposure during that period (Sioen et al. 2013). Recent research in animals indicates that there are low-dose mixture effects of POPs (Kortenkamp 2008). Cocktail exposures of animals at doses which individually do not produce adverse effects resulted in a high frequency of genital malformations and testicular impairment in the offspring (Christiansen et al. 2008). A few human studies have attempted to assess the effects of combined exposures of POPs, although these studies also point toward the possibility that the combined exposure rather than a single compound results in an adverse effect (Pierik et al. 2004; Damgaard et al. 2006; Main et al. 2007).

As it is summarized by WHO in 2012, numerous laboratory studies support the idea that environmental contaminants contribute to endocrine disorders in humans and wildlife. The most sensitive window of exposure to EDCs is during critical periods of development, such as during fetal development and puberty. Developmental exposures can cause changes that, while not evident as birth defects, can induce permanent changes that lead to increased incidence of diseases throughout life (Skakkebaek et al. 2007; WHO 2012).

Risk assessment

Estimated dietary intake assessments can be found in the literature (Kilic et al. 2011; Uçar et al. 2011), but there is no lifetime cancer risk assessment for PCBs in Turkey. Such an approach, with data from newborn bloods integrated to the risk assessment, will be an important base data in the evaluation of the general health concerns of humans in very critical periods of life, as well as for forthcoming studies about how endocrine disruptors affect humans. For this purpose, the non-dioxin-like, non-coplanar 2,2′,4,4′,5,5′-hexachlorobiphenyl (PCB 153) PCB congener which was found in high concentrations in human tissue and in other biological samples, as well as in the environment, was selected for pilot risk assessment approach. In human tissue, the total PCB concentrations in the blood were found to be consistent to those in blood, liver, muscle, kidney, and brain, where PCB 153 was one of the main ortho-substituted congener, accounting for approximately 27 % of the total PCBs in all the analyzed samples (Table 1). PCB153 does not have any significant dioxin-like toxicity due to the lack of binding to the aryl hydrocarbon receptor (AhR). Risk assessment over PCB153 may help to show the health hazard implicated in a long period, and also the results are discussible with international study results.

The Environmental Protection Agency of the USA (USEPA) has determined that PCB congeners should be categorized as probable human carcinogen (category B2), based on sufficient evidence of carcinogenicity in animals. The actual exposures are practically always known to be to PCB mixtures containing several congeners through diet in humans. Differences between congeners in absorption rates across the different exposure routes have minor effects on the toxicity. However, USEPA has concluded that in this stage, available evidence from human studies is inadequate but suggestive (EPA 1996; USEPA-IRIS 1997).

This study relies on the age-dependent response factors and cancer slope factor (ADAF and CSF) that have been established by EPA (EPA 1996, 2000, 2006, 2012, 2013; USEPA-IRIS 1997). Assessment of dose-response is not a cause of uncertainties in this study as the parameters used in our model have been assessed by USEPA based on evidence evaluated and published (EPA 1996; 1997), and they are used in our pilot model as such. In this study for cancer risk, excess risk of 10^{-5} was used for calculations (i.e., the probability of 1 in 100,000 that an individual may develop cancer from lifetime exposure to a carcinogen) (EPA 2000).

In order to understand the magnitude of exposure to POPs by infants, average daily intake was estimated based on the assumption that the average milk intake of a 5-kg infant is 700 g/day (Tsang et al. 2011). Mother's milk PCB 153 levels were estimated before by Çok et al. (2009) with the mean level of 8562 ng/g lipid. Mean daily intake of selected PCB was estimated using the following equation:

$$DI_{\text{milk}} = \left(C_{\text{milk}} \times 700\ \text{g} \times C_{\text{lipid}}\right)/5$$

where DI_{milk} is the estimated daily intake (ng/g body weight/day), C_{milk} is the concentrations of chemicals in milk (μg/g lipid weight), and C_{lipid} is the lipid content in milk (%) which was presumed as 3 %:

$$DI_{\text{milk}} = (8562\ \text{ng/g lipid} \times 700\ \text{g/day} \times 3/100)\ /\ 5\ \text{kg}$$

$$DI_{\text{milk}} = 0.0359\ \mu\text{g g}^{-1}\text{day}^{-1}$$

In risk assessment, risks to an individual have been assessed by dividing the total exposure into four intervals (default ADAF values are taken from EPA (EPA 2013)), as summarized at Table 3.

With birth, newborn has a load of PCB in the body as a result of pregnancy. This first load is also calculated as an internal dose, assumed to be only exposed for 1 day (day 0, birth) in lifetime. For the first 6 months, the cancer risk for exposure is computed as the function of estimated daily intake by breast milk. After 6 months, where breast feeding becomes

Table 3 Risk assessment assumed exposure factors

Age (years)	Exposure factors	Concentration (mg/kg)	IR, intake rate of the contaminated environmental medium for age (mg/kg)	BW, body weight (kg)	EF, exposure frequency for age bin (days/year)	ED, exposure duration (years)	AT, averaging time (days)	ADAF, age-dependent adjustment factor for age	SF, cancer slope factor (mg/kg-day)$^{-1}$
Day 0	İnternal dose	191.43 pg/g lipid	× 292.9 g		365/365	1 day	25,550	10	2
0–6 months	Child (breast feed)	0.0359 μg g^{-1}	day^{-1}		365/365	0.5	25,550	10	2
0.5–<2	Child	1070 pg/day/kg	bw		365/365	1.5	25,550	10	2
2–<16	Child/Adult	1070 pg/day/kg	bw		365/365	14	25,550	3	2
16–70	Adult	1070 pg/day/kg	bw		365/365	54	25,550	1	2

bw body weight

absolute, food becomes the main source of exposure. For each age interval "*i*," the cancer risk for exposure is computed as

$$Risk_{\mathrm{i}} = C.((IR_{\mathrm{i}}.EF_{\mathrm{i}}.ED_{\mathrm{i}})/BW_{\mathrm{i}}.AT).SF.ADAF_{\mathrm{i}}$$

where

C=concentration of the chemical in the contaminated medium (breast milk, food, etc.) to which the person is exposed. The unit is mg/kg.

IR_{i}=intake rate of the contaminated environmental medium for age bin "*i*." The unit is mg/day.

BW_{i}=body weight of the exposed person for age bin "*i*" (kg).

EF_{i}=exposure frequency for age bin "*i*" (days/year). This describes how often a person is likely to be exposed to the contaminated medium over the course of a typical year.

ED_{i}=exposure duration for age bin "*i*" (years). This describes how long a person is likely to be exposed to the contaminated medium during their lifetime.

AT=averaging time (days). This term specifies the length of time over which the average dose is calculated. For quantifying cancer risk, "lifetime" exposure employs an averaging time of 70 years (i.e., 70 years×365 days/year).

SF=cancer slope factor (mg/kg-day)$^{-1}$

$ADAF_{\mathrm{i}}$=age-dependent adjustment factor for age bin "i" (unitless).

Total risk to the individual is the sum of the risks across all four age intervals and internal dose established at newborn. So the calculations and assumption that have made are as below:

The estimated blood PCB153 mean level is 191.43 pg/g lipid in this study. Newborn body fat mass was estimated as 292.9 g which was estimated before by Harrod et al. (2014). PCB cancer slope factor (for high risk and persistence) by ingestion is 2 mg/kg-day (Abass et al. 2013). Dietary intake of total indicator PCBs for Turkish population (upper bound) is 1070 pg/day/kg body weight that was estimated before by Kilic et al. (2011). For high-risk assumption and because of persistency of congeners, total indicator PCB intake is used as $C \times IR$ without any change. Exposure duration per year is estimated as 365 days per 365 days, because the PCB congeners are ubiquitous and exposure is inevitable.

Assumed exposure factors and other data in risk assessment used are summarized in Table 3. Calculated risk factors for age groups are as follows:

Day 1 (internal dose)=4.4×10^{-8}
0–6 months=5.14×10^{-6}
6 months to 2 years=4.58×10^{-7}
2 to 16 years=1.28×10^{-6}
16 to 70 years=1.65×10^{-6}
Total risk=8572×10^{-6}

As the total risk for lifetime PCB exposure is below the acceptable risk, 10^{-5}, it may not be a significant factor for the

total burden cancer risk; however, authors are aware of the fact that cocktail effects may change it.

Today, we know that infancy is a critical period of development, and exposure to lipophilic environmental toxicants such as PCBs and OCPs in early life is an important determinant of long-term disease or disorder risks. Thus, we need large-scale epidemiological studies for understanding the contribution of these pollutants to the increased risk of unpredictable diseases in humans. Estimated dietary intake assessments can be found in literature, but this study as a pilot approach is the first one to show the lifetime cancer risk assessment for PCBs in Turkey. This information will be important base data for forthcoming epidemiological studies in the assessment of the general health concerns of newborns and communities.

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Compliance with ethical standards Participation of human subjects occurred after informed consent was received from each participant.

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