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PERINATAL EXPOSURE TO POLYCHLORINATED BIPHENYLS AND DIOXINS THROUGH DIETARY INTAKE.

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Abstract

Polychlorinated biphenyls (PCBs) and dioxins (polychlorinated dibenzo-*p*-dioxins and dibenzofurans) are potentially hazardous compounds. Since food is the major source (>90%) for the accumulation of PCBs and dioxins in the human body, food habits in women determine the degree of fetal exposure and levels in human milk. In order to investigate an association between dietary intake and PCB and dioxin levels in human milk and PCB levels in maternal and cord plasma, the food intake of 418 Dutch women during pregnancy was recorded using semi-quantitative food frequency questionnaires.

After adjusting for covariates, a weak association was found between the estimated dietary intake of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD), dioxins, and planar PCBs and their corresponding levels in breast milk. The estimated dietary intake of 2,3,7,8-TCDD, dioxins, and planar PCBs was also related to the PCB levels in maternal

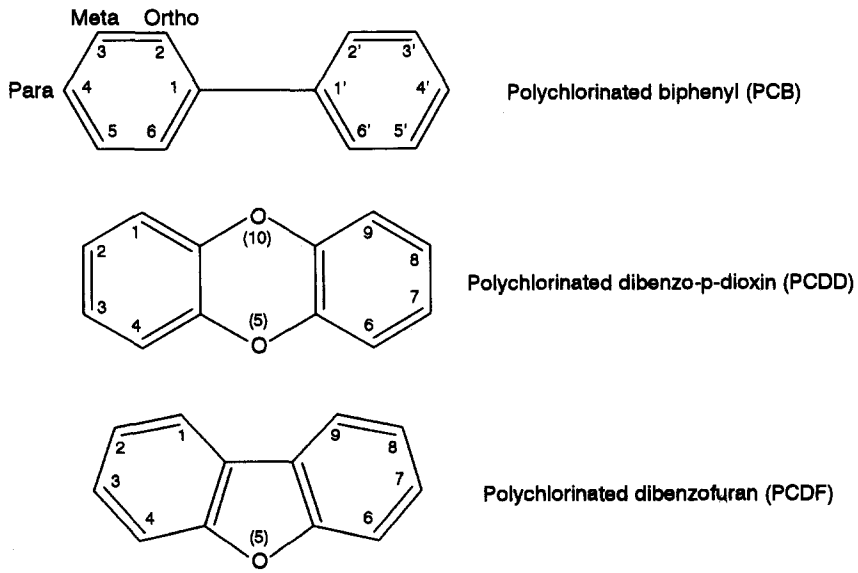
and cord plasma. Dairy products accounted for about half and industrial oils for about a quarter of the estimated 2,3,7,8-TCDD, dioxin, and the planar PCB intake.

It is concluded that the contribution of a pregnancy related diet to PCB and dioxin levels in human milk and to PCB levels in maternal and cord plasma is relatively low. Decrease of exposure to PCBs and dioxins of the fetus and the neonate probably requires long-term reduction of the intake of these pollutants. Substitution of normal cheese by low-fat cheese and the use of vegetable oils instead of fish oils in the preparation of foodstuffs by the food industry could contribute to a reduced intake of PCBs and dioxins.

Introduction

Polychlorinated biphenyls (PCBs) are a family of 209 congeners that differ in degree and place of chlorination. PCBs have electrical insulating properties. They are resistant to high temperatures and can conduct heat easily. PCBs have been widely used as plasticizers, fire retardants, in hydraulic fluids, and as dielectric fluids in capacitors and transformers[1]. PCBs can be divided into planar and non-planar PCBs. The planar PCBs do not have a chlorine atom in the ortho position of the biphenyl rings and resemble the dioxins (Figure I).

Figure I Molecular structures of PCBs, PCDDs, and PCDFs.



Polychlorinated dibenzo-*p*-dioxins (PCDDs) and dibenzofurans (PCDFs), summarized as dioxins, are tricyclic aromatic hydrocarbons. A PCDD congener has two bridges with two oxygen atoms; a PCDF congener has two bridges with one oxygen atom between the two aromatic rings. The number of chlorine atoms range from one to eight. Although 210 PCDD and PCDF congeners can be formed, only the seventeen congeners with a 2,3,7,8-substituted pattern are usually found in biotic samples. From these 2,3,7,8-substituted congeners, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) is the most toxic. Dioxins are unwanted byproducts of industrial and thermal processes. In the Netherlands, the incineration of municipal and industrial waste is the most important source for atmospheric deposition[2]. Both PCBs and dioxins are persistent environmental pollutants. Background levels of PCBs and dioxins have been reported in air, water, soil, and sediment. They are lipophilic and chemically stable[3] and have become part of the food chain. In western industrial countries, considerable amounts have been found in fish, meat, dairy products and, in particular, in human milk[4].

In the case of no direct exposure, such as skin contact or inhalation, food seems to be the major source (>90%) of human exposure to PCBs and dioxins[5-7]. Most of the PCB and dioxin congeners will be absorbed and eventually stored in adipose tissue. The half-lives of the congeners are fairly long, for instance 12 years for 2,3,7,8-TCDD[8]. On a lipid basis, PCB and dioxin contents in blood and adipose tissue (including human milk fat) are similar. During pregnancy, PCBs and dioxins are able to cross the placenta[9-11]. In plasma, PCB concentrations on a lipid basis are similar on both sides of the placenta[12]. Because of the accumulation in the human body, maternal food habits up to the age of reproduction are of great importance to determine the degree of fetal exposure and levels in human milk. There are indications of long-term negative effects of fetal and neonatal exposure on behavioral and early cognitive development[13] and on fertility[14].

Jacobson *et al.*[15] followed 242 newborns whose mothers consumed PCB-contaminated fish from Lake Michigan and found a lower neonatal behavioral performance than in 71 control infants whose mothers did not eat fish. Prenatal PCB exposure was also associated with poorer visual recognition memory at 7 months[16].

We have reported that pre- and early postnatal exposure to PCBs, PCDDs, and PCDFs is related to neurological optimality and incidence of mild hypotonia in newborns[17]. In infants of mothers with high PCB and dioxin levels in their breast-milk, an increase of non-optimality and mild hypotonia was found. In the present study of the same

cohort, we investigate whether dietary intake of women during pregnancy was associated with PCB levels in maternal and cord plasma and with PCB and dioxin levels in human milk. Feasible measures to reduce dietary intake of PCBs, PCDDs, and PCDFs are proposed.

Methods

Study design

From June 1990 until June 1992, a study population of 418 Dutch mother-infant pairs was recruited in the Groningen and the Rotterdam areas. Two hundred and nine infants were breast-fed and an equal number was formula-fed. The methods of this study have been reported previously[17,18].

Dietary intake

In the sixth week after delivery, the 211 Groningen and 207 Rotterdam mothers were asked to complete a semi-quantitative food frequency questionnaire about their food habits during pregnancy. This questionnaire was validated by comparison with dietary history[19]. It includes frequency and quantity of food products consumed. The food intake calculations were performed by dieticians using different computer programs (VOBEMA/Hanzehogeschool in Groningen, and Becel dietary program in Rotterdam). Both are based on the Dutch Nutrient Database[20] and allow calculation of macronutrient intake (daily energy, protein, carbohydrate, and fat intake).

Twenty-five food categories were constructed in Groningen according to Liem *et al.* (1991). Of the initial food categories, 19 categories were included in the analysis. The questionnaire could not distinguish between liver from cows, pigs, or chickens; these 3 food categories were combined into one category. The women did not report game, mutton, soya bean oil and horse meat and therefore these 4 categories were deleted. Industrial oils are a mixture of vegetable, animal and fish oils and are used by the food industry in the preparation of various foodstuffs e.g. savoury snacks, mixed dishes, sauces, pastry, cakes and biscuits. In Rotterdam, 12 food categories were constructed. Nuts, sunflower oil, vegetable oil, cereals, and fruit/vegetables were combined into one category. Industrial oils were not calculated in Rotterdam as a separate food category but were included in the categories meat, fish, and vegetable oils.

To estimate the dietary intake of 2,3,7,8-TCDD, dioxins, and planar PCBs,

calculations were made using reference data for food products, as provided by the Dutch National Institute of Public Health and Environmental Protection (RIVM)[21]. The RIVM used the toxic equivalence factor (TEF) approach[22] to calculate a toxic equivalent (TEQ) value for each food category. In Groningen, the calculated fat content per food category was multiplied by the TEQ values from the RIVM, whereas in Rotterdam, the calculated fat content per food item was used. In Groningen, the TEQ intake is the sum of the TEQ values of all food categories, whereas in Rotterdam, the TEQ intake is the sum of the TEQ values of all food items.

In order to examine the possible effect of certain feasible dietary changes aiming to reduce the total TEQ intake, we have estimated the consequences of a modified intake.

Samples and analytical methods

Maternal blood was collected in the last month of pregnancy and cord blood immediately after birth. In plasma samples only the four non-planar PCB congeners 118, 138, 153, and 180 could be analysed due to the small available volume of plasma. The sum of the four congeners (ΣPCB) in plasma was used in the statistical analyses. In the second and 6th weeks after delivery, the women who breast-fed their infants collected a 24-hour sample of breast milk. In breast milk, 17 dioxin and 3 planar PCB congeners were analysed. In addition, twenty-three non-planar PCB congeners were measured in these milk samples. The analytical methods have been reported elsewhere[17,18].

Statistical analysis

For a univariate comparison of the dietary constituents, and PCB and dioxin intake between the study centres, we used chi-square, Student's t, and the Mann-Whitney U tests (two-tailed). Multiple linear regression analysis was used to investigate relations between plasma PCB levels, and PCB and dioxin levels in human milk as the dependent variables and dietary intake of 2,3,7,8-TCDD, dioxins, and planar PCBs as the independent variables. Adjustments were made for the variables of the recorded obstetrical optimality list[23]. If necessary, the levels were logarithmically transformed. All tests were performed at the 5% significance level.

Results

The questionnaire about food habits during pregnancy was completed by 397 women (211 in Groningen and 186 in Rotterdam). A higher intake of energy, protein and fat was found in Rotterdam as compared to Groningen (Table I). The observed differences were fairly large. Therefore, we reviewed the dietary data collection process in the two centres. We randomly selected 10 questionnaires from each centre and sent these for processing to the other centre. Analysis of these questionnaires revealed differences: The macronutrient intakes were on average estimated higher in Rotterdam than in Groningen. The analysis did not reveal a specific pattern of differences. However, it was not possible to re-assess all the questionnaires. The recorded intakes are thus subject to a considerable measurement error.

Table II shows dietary intake of 2,3,7,8-TCDD, dioxins, planar PCBs, and total TEQ during pregnancy. None of the estimated dietary intakes exceeds the Dutch tolerable daily intake (e.g. 10 pg TEQ/kg body weight[24]).

Three maternal blood samples were missing. No cord blood samples could be obtained from 36 mother-infant pairs. For the analysis of PCB 118 in cord plasma, nine samples were missing. For human milk, dioxin -, and planar PCB TEQ values were available in 171 and 188 samples, respectively. The PCB concentrations in plasma and the PCDD and PCDF contents in breast milk have been reported elsewhere[17,18].

After adjusting for age, age^2, Quetelet index (weight/length^2), energy intake, alcohol consumption during pregnancy, and study centre, we found a significant relation between the ΣPCB in maternal and cord plasma, and the dietary intake of planar PCBs (Table III). Nearly the same results are obtained if the dietary intake of planar PCBs is replaced by the 2,3,7,8-TCDD or the dioxin intake. In Table IV, after adjusting for age, age^2, energy intake, and study centre, a significant relation is demonstrated between the dietary intake of 2,3,7,8-TCDD, dioxins, and planar PCBs and their corresponding levels in breast milk. Closer examination of the coefficients for age and age^2 reveals that the positive effect of age tends to diminish.

Table I Daily intake of energy and macronutrients during pregnancy in Groningen and Rotterdam.

	Groningen (n=211)			Rotterdam (n=186)		
	Percentiles			Percentiles		
	P5	P50	P95	P5	P50	P95
Energy (kJ/d)*	8,680	10,350	11,970	7,730	11,000	16,560
Protein (g/d)*	65	88	113	65	94	140
Carbohydrate (g/d)	239	304	378	191	286	457
Fat (g/d)*	72	103	130	80	120	182

** Significantly higher in Rotterdam ($p \leq 0.05$).*

Table II Dietary intake of 2,3,7,8-TCDD, dioxins, planar PCBs and total TEQ during pregnancy.

		Study group (n=397)		
		Percentiles		
		P5	P50	P95
2,3,7,8-TCDD	pg TEQ/d	7.3	12.9	21.5
	pg TEQ.BW/d†	0.11	0.20	0.37
Dioxins	pg TEQ/d	42.1	76.4	122.0
	pg TEQ.BW/d†	0.60	1.19	2.10
Planar PCBs	pg TEQ/d	55.0	100.5	169.1
	pg TEQ.BW/d†	0.80	1.58	2.78
Total TEQ*	pg TEQ/d	97.4	177.6	288.3
	pg TEQ.BW/d†	1.45	2.77	4.88

** total TEQ = dioxin TEQ + planar PCB TEQ*

† pg TEQ per kg body weight per day

Table III Results of multiple regression analysis: maternal and cord plasma.

	Log(ΣPCB) in	
	Maternal plasma b (se)	Cord plasma b (se)
Constant	0.132 (1.24)	−0.161 (1.57)
Planar PCB intake† (pg TEQ/week)	0.247* (0.060)	0.281* (0.075)
Age (years/10)	1.950* (0.540)	1.883* (0.693)
Age^2	−0.272* (0.092)	−0.269** (0.118)
Quetelet index	−0.0177* (0.0052)	−0.0358* (0.0067)
Energy intake† (kJ/d)	−0.435* (0.105)	−0.550* (0.135)
Alcohol consumption during pregnancy (0=no, 1=yes)	0.118* (0.041)	0.194* (0.053)
Study centre (0=Groningen, 1=Rotterdam)	0.052 (0.036)	0.152* (0.046)
n; R^2	395; 0.31	355; 0.31

ΣPCB = sum of PCB 118, 138, 153 and 180; b = regression coefficient; se = standard error; † = logarithmically transformed; R^2 = fraction of explained variance.

** $P < 0.01$.*

*** $P < 0.05$.*

Table IV Results of multiple regression analysis: human milk.

	Human milk		
	2,3,7,8-TCDD† b (se)	Dioxins† b (se)	Planar PCBs† b (se)
Constant	0.162 (2.757)	2.288 (2.082)	0.902 (2.714)
2,3,7,8-TCDD intake†	0.343* (0.107)		
Dioxin intake†		0.343* (0.094)	
Planar PCB intake†			0.363* (0.110)
Age (years/10)	3.245** (1.324)	2.467** (1.045)	2.723** (1.324)
Age^2	−0.505** (0.220)	−0.379** (0.174)	−0.444** (0.220)
Energy intake† (kJ/d)	−0.610* (0.196)	−0.550* (0.151)	−0.514* (0.195)
Study centre (0=Gron, 1=Rot)	0.250* (0.064)	0.121** (0.050)	0.032 (0.066)
n; R^2	167; 0.23	171; 0.21	188; 0.12

Dietary intake in pg TEQ/week; b = regression coefficient; se = standard error; † = logarithmically transformed; R^2 = fraction of explained variance.

** $P < 0.01$.*

*** $P < 0.05$.*

Table V shows the relative contribution of food categories to the intake of 2,3,7,8-TCDD, dioxins, and planar PCBs in Groningen and Rotterdam. The consumption of cow's milk and cheese is responsible for about 18% and 19% of the 2,3,7,8-TCDD intake, respectively. The same categories are responsible for 24% and 18% of the dioxin intake and for 17% and 20% of the planar PCB intake, respectively. Industrial oils are responsible for about 24%, 19%, and 26% of the 2,3,7,8-TCDD intake, the dioxin intake, and the planar PCB intake, respectively (These data were available for the Groningen group only).

Table V Relative contributions to 2,3,7,8-TCDD, dioxin, and planar PCB intake from food categories in Groningen and Rotterdam (n=397).

	Dietary intake (%)		
Source	2,3,7,8-TCDD	Dioxins	Planar PCBs
	Median (P25-P75)	Median (P25-P75)	Median (P25-P75)
Dairy*	47 (37-57)	53 (42-63)	53 (42-58)
Cow's milk	18 (12-26)	24 (17-35)	17 (11-25)
Cheese	19 (11-28)	18 (10-28)	20 (11-30)
Other†	53 (43-64)	47 (37-58)	52 (42-63)
Industrial oils‡	24 (18-31)	19 (14-24)	26 (19-35)

** Dairy = cow's milk + cheese + butter*

† Other = beef + liver + pork + mixed meat products + poultry + lean fish + fatty sea fish + eel + fresh water fish + eggs + nuts + sunflower oil + vegetable oil + cereals + fruit/vegetables + industrial oils.

‡ Data available for the Groningen group only (n=211).

Discussion

The food habits of 397 pregnant women were evaluated in two different areas of the Netherlands: Groningen, a semi-urban area in the northeast, and Rotterdam, a highly industrialized region in the southwest of the Netherlands. Apart from dietary intake, the

women did not report having been exposed to PCBs and dioxins. The estimated dietary intake of 2,3,7,8-TCDD, dioxins, and planar PCBs during pregnancy was significantly related to their corresponding levels in breast milk and also to the PCB levels in maternal and cord plasma.

In dietary intake surveys in Germany[25] and in the Netherlands[21], a median daily dioxin intake about 1.2 pg TEQ/kg body weight was found. Our results are similar (Table II). For dioxins, we found a contribution of 53% from dairy, compared to 45% reported by Liem *et al.*[21] In Germany, dairy consumption seems to be lower and accounts for 30% of the average dioxin intake[5].

Although food is generally accepted as the major source of PCB and dioxin intake[5-7], in the present study, the proportion of variance explained by food intake was low. The main reason for this is probably the fact that the semi-quantitative food frequency questionnaire does not provide information on long-term dietary intake. Individual differences in the absorption, body distribution and metabolism may also be involved. The proportion of variance is also negatively influenced by errors in measuring dietary intake.

Compared to placental transport, the total quantity of PCBs and dioxins transferred to a baby via breast milk is considerable[26]. In a breast-fed baby weighing 5 kg with a daily consumption of 800 mL milk with 3% fat, the median daily intake would be 222 pg TEQ/kg body weight (in the present cohort, the median dioxin and planar PCB TEQ value in human milk was 30.2 and 16.1 pg TEQ/g fat, respectively[17]). This daily intake of dioxin-like compounds is about 20 times higher than the Dutch tolerable daily intake[24]. On a body weight basis, it is about 80 times higher than the median intake of an adult (Table III).

The question arises whether it is possible to reduce the PCB and dioxin exposure via food intake. Pluim *et al.*[27] demonstrated that short-term dietary alterations did not reduce dioxin levels in breast milk. They suggested that only prolonged consumption of food with a low PCB and dioxin content will reduce adipose tissue levels and consequently the fetal exposure and the levels in human milk fat. This is in accordance with our findings that the age of the mother is related with the PCB and dioxin levels in breast milk (Table IV). This indicates a continuous influx of PCBs and dioxins during the course of life, which can probably be altered by long-term reduction of the intake of these pollutants only.

In the present study, dairy products and industrial oils are the major contributors to the daily intake of dioxins and planar PCBs (Table V). Two modest dietary alterations will lower the intake of PCBs and dioxins that is replacement of the usually consumed normal cheese (48% fat) by low-fat cheese (20% fat), and the use of vegetable oils instead of contaminated fish oils in the preparation of foodstuffs by the food industry. Fish oils, together with vegetable and animal oils are used by the food industry in the preparation of various foodstuffs. These fish oils account for more than 95% of the quantity of PCBs and dioxins in industrial oils[21,28]. Because of their polyunsaturated fatty acid content, fish oils are expected to have beneficial effects[29]. Unfortunately, the possible beneficial effects disappear during the preparation process (hydrogenation). Due to the development of the prices on the world market, the contribution of fish oils to industrial oils in the Netherlands decreased from about 18% in 1988[30] to about 12% in 1990 and to about 5% in 1993[31]. In view of these large changes, a total abolition of the use of contaminated fish oils in industrial oils appears feasible.

We have estimated the consequences of the above described modified intake. Consumption of low-fat cheese instead of the normal one is estimated to result in a median reduction of 11% (range: 0-43%) of the PCB and dioxin intake. The median reduction due to abolition of the use of fish oils in industrial oils is estimated as 22% (range: 5-78%).

In conclusion, the estimated dietary intake of 2,3,7,8-TCDD, dioxins, and planar PCBs during pregnancy is weakly related to levels in breast milk and to PCB levels in maternal and cord plasma. A substitution of normal cheese by low-fat cheese and the use of vegetable oils instead of fish oils in the preparation of foodstuffs by the food industry could contribute to a lower intake of PCBs and dioxins. In the long run, this would reduce fetal exposure and neonatal exposure through breast-milk.

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