THE DUTCH PCB/DIOXIN STUDY

Influence of maternal dietary habits on the pre- and postnatal exposure to xenobiotics.

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Introduction

Seven institutes in the Netherlands (Academic Hospital Groningen, Sophia Children's Hospital Rotterdam, Agricultural University Wageningen, MBL-TNO Rijswijk, IBC-TNO Zeist, ITV-TNO Zeist and RIKILT-DLO Wageningen) are collaborators on a project which studies the long-term effects of early (fetal/neonatal) exposure to polychlorinated biphenyls (PCBs) and dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs). This study includes both human and animal studies. The project is funded by the Dutch Government from various sources. The clinical segment of the study is managed by the Academic Hospital Groningen (Depts. Obstetrics and Developmental Neurology) and Erasmus University/Sophia Children's Hospital, Rotterdam.

Physical examination, growth, and neurodevelopmental parameters are recorded during the first 36 months of life and compared with the levels of exposure in utero or through breast milk. Within the framework of this study, we will report on the maternal dietary habits of a sub-population in relation to their PCB/dioxin concentrations in their milk fat, maternal plasma, and in cord plasma. Additionally, the concentration of the PCB congeners (153, 138, 180, and 118) found within maternal and cord plasma is presented.

Methods

In order to examine the health risks associated with postnatal exposure to PCBs and dioxins, exclusively breast-fed infants are compared with infants fed on a formula. These groups are chosen because of the relatively high content of these xenobiotics in breast milk as compared to formula. Fetal exposure is determined by the background contamination of the PCB congeners (153, 138, 180, and 118) in cord plasma and in maternal plasma at 36th week of gestation. Throughout the duration of the study, the obstetrical optimality score[1] has been recorded of all mothers. This score consists of 76 items relating to the socio-economic background, the antenatal, intrapartum, and postnatal condition (e.g. the duration of gestation, parity, maternal age and Quetelet index, birthweight etc.). The dietary study of the mothers was based on a sub-sample (n=211) of the population of residents in the Northern part of the Netherlands (Groningen). The study was administered on the basis of informed consent. Results for the Southern, more industrialized part of the Netherlands (Rotterdam area) are still being prepared. In order to be included in the study, pairs of mothers and infants had to meet the following criteria: only first or second born term infants (37-42 weeks of gestation) of caucasian parents with the Dutch nationality were included. An instrumental delivery was excluded. Exclusively breast-feeding mothers (n=104) were compared with those mothers who gave their infants bottle-feeding (n=107). After obtaining instructions from one of the researchers (M.H.), the women, in their 6th week following delivery, completed a slightly adapted semi-quantitative food frequency questionnaire for use in epidemiological research. This questionnaire has been validated by comparison with dietary history[2]. The food intake calculations were performed using a computer program based on a Dutch nutrient database (VOBEMA/Hanzehogeschool, Groningen using the NEVO tables, CIVO/TNO). In order to estimate the dietary intake of dioxin and dioxin-like planar PCBs, calculations were made with the help of the reference data provided by the RIVM for 'Dutch' foodproducts[3]. The calculated PCB/dioxin consumption in both groups of women was an application of the international accepted toxicological equivalence factors (TEF) for dioxins and proposed TEFs for the PCBs. Through the summation of these products, the toxicity of a mixture was calculated and expressed in pg toxic equivalents (TEQ) per kg body weight per day. Breast milk was collected as a representative 24 hrs sample at 10 days, 6 weeks, and if possible, 3 months after delivery. In breast milk, dioxin and planar PCB congeners were measured by capillary gas chromatography with electron capture and mass spectrometric detection[4]. Maternal plasma was collected in the 36th week of pregnancy. A previous study showed that PCB levels at week 36 of gestation were comparable with values immediately prior to delivery. Triglycerides (TG) in maternal plasma and cord plasma were determined through an enzymatic method (SMAC).

Results

Significant differences in social background between the parents of the breast feeding (BF) and formula-feeding (FF) group were found. As expected for the Dutch situation, women in the BF group, her partner, and her father recieved a higher education. In the FF group, the percentage of smoking during pregnancy was higher for both the woman and her partner. Mean age of the women in the FF group was significantly younger (27.9 yrs) as compared to those of the BF group (30.4 yrs). Mean weight was higher for the women of the FF group (66.7 kg) than in the BF group (63.5 kg), however the Quetelet index (weight/length^2) were similar.

Dietary consumption pattern revealed no differences in the energetic and total fat intake between the BF and FF group. However, the protein consumption was higher ($p<0.0001$) and carbohydrate intake lower ($p<0.05$) in the BF group of women. Intake of dioxins and planar PCBs was higher in the BF group of women ($p<0.001$) mainly due to an increased consumption of **cow's milk** ($p<0.05$), **cheese** ($p<0.0001$), **butter** ($p<0.05$) and **beef** ($p<0.05$). Women in the FF group consumed more pork ($p<0.0001$) and (vegetable) oil ($p<0.001$). Consumption of liver, chicken, eggs, nuts, and fish were similar in both groups of women.

Regarding the planar PCBs, the BF group of women consumed, on average, 1.68 pg TEQ per kg bw per day, significantly higher ($p<0.001$) than the FF group (1.31). These results are comparable to the dioxin the BF group consumed, namely 1.52 pg TEQ; remarkably higher than the FF group (1.20 pg TEQ per kg bw per day; $p<0.001$). We found a direct correlation between the intake and the contamination levels in breast milk, maternal, and cord plasma (not shown). PCB congeners (153, 138, 118, and 180) in maternal plasma and their corresponding levels on the other side of the placenta (cord plasma) are depicted in Table I for both the BF and the FF group of mother and infant pairs. Significantly higher levels were found in the women of the BF group. A similar trend was recorded for the cord plasma levels. Mean levels of the individual congeners on the maternal side are approximately 5 times as high as those on the fetal side (cord plasma). TG levels in cord plasma were approximately 20% of those in maternal plasma, during the last part of pregnancy. Since PCBs are fat soluble and mainly transported by triglycerides with lipoproteins, levels of the individual PCB congeners were also calculated per TG content in maternal plasma and in cord plasma (not shown). In contrast to the PCBs in whole plasma (Table I), mean levels of PCB 153 and 138 calculated per TG content were similar in maternal and cord plasma. This may indicate an equilibrium between the two major PCB containing fat compartments in blood on both sides of the placenta.

Conclusion

In reference to the Northern Netherlands, it appears as though breast-feeding mothers do smoke less but are older, receive more education, and consume a diet which contains

more xenobiotics than her counterpart who formula-feeds her infant. Typical for their lifestyle, not fish, but milk products, including cheese, are important sources of xenobiotics contributing to relatively high concentrations in her adipose tissue, and thereby in milk fat. A relatively high consumption of these xenobiotics is also reflected in an increased fetal exposure to these products as compared to those mothers who formula-feed their children. It is apparent, that in the Netherlands, more attention must be paid to reduce the exposure of cows to these toxic compounds.

References:

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TABLE I

Mean levels (SD) of PCB 153, 138, 118, and 180 (ng/ml) in maternal and cord plasma of the breast-feeding group (BF) and the formula-feeding group (FF)

	Maternal plasma			Cord plasma		
	BF-group n=95	FF-group n=56	P*	BF-group n=74	FF-group n=37	P*
PCB 153	1.02 (0.40)	0.80 (0.28)	<0.001	0.19 (0.09)	0.16 (0.07)	n.s.
PCB 138	0.62 (0.28)	0.54 (0.18)	<0.001	0.13 (0.06)	0.12 (0.05)	n.s.
PCB 118	0.19 (0.09)	0.15 (0.07)	<0.001	0.05 (0.02)	0.04 (0.02)	<0.05
PCB 180	0.61 (0.23)	0.47 (0.15)	<0.001	0.10 (0.04)	0.08 (0.04)	<0.05

*Student's t-test, used with log. concentrations; n.s. =not significant.