EFFECT OF PERINATAL EXPOSURE TO ENVIRONMENTALLY PERSISTENT ORGANIC POLLUTANTS AND HEAVY METALS ON NEUROBEHAVIORAL DEVELOPMENT IN JAPANESE CHILDREN: PCBS EXPOSURE AND NEONATAL NEUROBEHAVIORAL STATUS

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Introduction

The neurobehavioral effects of perinatal exposures to methylmercury (MeHg) and environmentally persistent organic pollutants (POPs) including polychlorinated biphenyls (PCBs), dioxins and pesticides are of great concern world wide. Several epidemiological studies have reported some associations of perinatal exposure to MeHg or PCBs with neurobehavioral deficit, such as postnatal growth delay and poorer cognitive functions[1]. These chemicals accumulate in human body mostly through the consumption of food, especially fish and shellfish. On the other hand, since fish is rich in nutrients such as polyunsaturated fatty acid (PUFA) essential for normal brain development of fetus, fish has been usually recommended for pregnant women. Therefore, from perspective of risk assessment, these health hazard issues are important for fish eating populations.

We have been performing a prospective cohort study, the Tohoku Study of Child Development (TSCD), to examine the effects of perinatal exposure to MeHg, PCBs, and dioxins on neurobehavioral development in Japanese children[2]. We registered 599 mother-infant pairs from January 2001 to September, 2003 in an urban area of Tohoku district, Japan. Samples such as maternal peripheral blood, cord blood, breast milk and maternal hair were collected for chemical determination. For the assessment of neurobehavioral development, Brazelton Neonatal Behavioral Assessment Scale (NBAS) was administered when children were three days old, and other tests including Bayley scales of infant development second edition and Kaufman assessment battery for children were performed with growth of children.

In the present study, we report the preliminary results on the association of NBAS with total PCB concentration in cord blood and maternal fish intake.

Materials and Methods

Participants were 163 mother-infant pairs whose variables including PCBs concentration in cord blood, NBAS, and other covariates were available. Mean maternal age at the delivery was 31.9 (SD4.2). Infants consisted of 87 boys and 76 girls, and they were all singleton and full-term (36-42 weeks) gestation without congenital anomalies or diseases. Birth weight was 2400g or more. Information was obtained about pregnancy, delivery conditions and infant characteristics from medical record.

PCBs concentration was measured from whole of cord blood collected immediately after delivery. All 209 congeners were analyzed using HR-GC/MS (Metocean environmental Inc, Shizuoka, Japan). Total PCB concentration represented the sum of the all measured congeners, expressed as ng/g-fat.

Maternal fish intake was estimated using the semi-quantitative food frequency questionnaire (FFQ) for 122 individual foods and recipes[3] and 13 additional items regarding fish and shellfish. The FFQ was administered at four days after delivery. Trained investigators showed mothers a real size photograph of each food, then, mothers answered the frequency and the amount of intake per meal.

For other variables of chemical analysis, hair mercury (hair Hg) concentration was analyzed from maternal hair samples taken at two days after delivery. Total hair Hg concentration was measured by cold vapor atomic absorption[4] at National Institutes of Minamata Disease (Minamata, Japan). Thyroid hormones including thyroid-stimulation hormone (TSH), total thyroxine (T4), triiodothyromine (T3), free T4 and free T3, were measured from plasma of cord blood by SRL, Inc. (Tokyo, Japan).

NBAS was administered on three days after delivery. Examiners of the NBAS were trained and certified at the training center for NBAS in Nagasaki University School of Medicine, Japan. Reliability check was conducted throughout the data collection to maintain a 90% level of agreement.

In the statistical analysis, a stepwise multiple regression analyses were performed for adjustment of covariates. The potential covariates were as follows; maternal age at delivery, maternal alcohol drinking during pregnancy, maternal smoking habit, maternal total energy intake, delivery type, parity, gestational age, gender, birth weight, apgar score, TSH and T3 concentration in cord blood, maternal hair Hg concentration, and NBAS examiners. The significance level was set at 5%.

Results and Discussion

The mean total PCB concentration in cord blood was 65.3 ng/g-fat (SD 43.4), and the mean maternal total fish intake was 2.6 kg/year (SD 1.6). Table 1 shows results of multiple regression analyses. A positive

association was found between total PCB concentration and the score of the regulation of state cluster. A negative association was found between total fish intake and the score of the habituation cluster.

Early studies reported the negative associations of prenatal PCBs exposure with neurobehavioral development. We hypothesized the negative associations between total PCBs in cord blood and the NBAS. On the other hand, because fish is rich in nutrients such as PUFA essential for brain development, we also hypothesized the beneficial effects of maternal fish intake on the neonatal neurobehavioral status. Our findings are not in line with our hypotheses and the findings from early studies. We do not know clearly the reason for these findings, there are several possibilities. First, it is possible that the level of PCB exposure in our study was too low to detect the effects of PCB exposure on neonatal neurobehavioral status. We supposed that the level of PCB exposure in our study might be lower than those of early studies[5, 6, 7], although it is difficult to compare PCB levels among studies for different analytical methods. Second, since this report is based on the preliminary results, the sample size too small to detect the effects of low level exposure to PCB. The entire participant of our cohort study is 599 mother-infant pairs, and we collected not only samples of cord blood, but also maternal peripheral blood and breast milk. The measurements of chemicals including PCBs are now on going, and the further study will reveal the associations of neurobehavioral development with perinatal PCBs exposure and fish intake.

Table 1. The results of multiple regression analyses

	Habituation	Orientation	Motor	Range of state	Regulation of state	Autonomic stability	Reflex
Total PCBs (ng/g-fat)[1]	0.47	0.34	0.28	-0.04	0.81*	0.16	-1.39
Total fish intake (kg/year)[1]	-0.87*	-0.00	0.20	-0.34	0.73	-0.23	-0.28

(Beta value) * $p < .05$

[1]Log translations, $Log_{10}X$, were used on the value of total PCB concentration and total fish intake.

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