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Review

The Duisburg birth cohort study: Influence of the prenatal exposure to PCDD/Fs and dioxin-like PCBs on thyroid hormone status in newborns and neurodevelopment of infants until the age of 24 months

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Abstract

Prenatal exposure to polychlorinated biphenyls (PCBs) and polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs) can affect neurobehavioral development of infants and children. This effect may be mediated through disruption of thyroid hormone homeostasis. However, epidemiological studies reveal no consistent influence of PCDD/Fs and PCBs on thyroid status and neurodevelopment at environmental background levels. The effects may resolve with time of further decreasing exposure to these compounds. The aim of this study was to find out if there are still effects related to prenatal PCDD/F and PCB observable at the meanwhile decreased levels of exposure by using the same methods which have been applied in similar studies during the last 10 years in Europe. The birth cohort study was initiated in the year 2000 in the industrialized city of Duisburg, Germany. 232 healthy mother–infant pairs were recruited between 2000 and 2002. Dioxins, dioxin-like PCBs and six indicator PCBs were analyzed in maternal blood during pregnancy and in maternal milk following extraction and sample clean-up by HRGC/HRMS. Thyroid stimulating hormone (TSH), total thyroxine (T4), total triiodothyronine (T3), free thyroxine (FT4) and free triiodothyronine (FT3) were measured in serum samples of the pregnant women and in cord serum samples by chemiluminescent immunometric assay. Neurological examinations were performed at ages 2 weeks and 18 months using the neurological optimality score (NOS), mental and motor development were assessed using the Bayley Scales of Infant Development (BSID) at ages 12 and 24 months. Multiple linear regression analysis was used to describe the association of PCDD/F and PCB in maternal blood or milk with the outcome measurements after adjustment for confounding. Blood levels ($n = 182$) of WHO 2005 toxic equivalents (TEQ) (PCDD/F + PCB) were in the range of 3.8–58.4 pg/$g_{\text{lipid base}}$ (median: 19.3 pg/$g_{\text{lipid base}}$). The corresponding data for human milk ($n = 149$) were 2.6–52.4 pg/$g_{\text{lipid base}}$ (median: 19.7 pg/$g_{\text{lipid base}}$). Multiple regression analysis showed no decrease of thyroid hormones related to WHO 2005 TEQ in blood and milk of mothers and their newborns. Furthermore, no associations between exposure and neurological and developmental measures were observed. This study supports the view that the current decreased exposure to PCDD/Fs and PCBs does not impair thyroid function of newborns and neurodevelopment of infants until the age of 24 months.

Keywords: Birth cohort study; PCDD/Fs; Dioxin-like PCBs; Thyroid hormones; Neurodevelopment; WHO 2005 TEQ; Blood; Breast milk

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Contents

1. Introduction

Polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs), shortly dioxins, and polychlorinated biphenyls (PCBs) are persistent organic pollutants (POPs). Negative effects of prenatal and perinatal exposure to PCDD/Fs and PCBs on neurodevelopment have been documented in many studies and the results have been summarized in reviews [1–3]. Due to worldwide efforts of reduction or even elimination the exposure of the general population to PCDD/Fs and PCBs has decreased during the last years [4]. However, several birth cohort studies have shown that developmental neurotoxicity may be associated with prenatal, perinatal and/or postnatal exposure to POPs even at background environmental levels, but the results are inconsistent. At rather high background environmental levels during the 1960s, in utero PCB exposure of children born in the years 1964–1967 in California (USA) was associated with reduced fetal growth [5]. In the North Carolina (USA) study (year of start 1978–1982) transplacental exposure to PCBs was associated with lower psychomotor scores using the Bayley Scales of Infant Development (BSID) at both 6 and 12 months of age [6]. Transplacental PCB exposure had no influence on the mental scores and the postnatal PCB exposure by breastfeeding had no deleterious effects. In 1990 the Rotterdam and Groningen (The Netherlands) studies were started to investigate the effects of perinatal and postnatal exposure to background levels of PCBs and dioxins on growth and development [3]. Exposure through breast milk to PCBs, PCDD/Fs was associated with a reduced neonatal neurological optimality [7]. But the levels of 4 non-planar PCBs in cord and maternal plasma were not related to neurological function. At 18 months, however, prenatal PCB as measured by PCB in cord and maternal plasma was negatively related to the neurological examinations while levels of PCB and dioxins in milk had even a somewhat beneficial effect [8]. The results on infant's motor and psychomotor development of the Dutch study were as follows [9]. Prenatal PCB exposure had small negative effect on the psychomotor score at 3 months of age. PCB and dioxin exposure through breastfeeding had an adverse effect on the psychomotor outcome at 7 months of age. There was no influence of the perinatal PCB and dioxin exposure on the mental development at ages 3 and 7 months. At 18 months of age perinatal PCB and dioxin exposure did not affect neurodevelopment. Continued follow-up of this cohort suggested that adverse cognitive effects were observed at 42 months of age and were even still detectable at the age of 9 years in children from socially disadvantaged families [10]. The effects on auditory P300 latencies were different for prenatal PCB exposure and PCB exposure via breastfeeding [11]. In the Düsseldorf (Germany) birth cohort study which was initiated in 1993, PCB levels in milk were negatively associated with mental and motor development as assessed by the BSID in infants at the age of 7, 18, and 30 months [12]. The follow-up of the Düsseldorf cohort demonstrated that, by using the Kaufmann Assessment Battery for Children, PCB-related cognitive impairment was also observable at the age of 42 months but no longer at the age of 72 months [12,13]. In the Collaborative Perinatal Project, in which pregnant women from 12 US study centers were included, no clear association of the prenatal exposure to background levels of PCBs as measured by PCB concentrations in maternal third trimester sera on mental and motor development (measured by the BSID) at 8 months