Environment International 36 (2010) 649–654

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Metal exposures in an inner-city neonatal population

Elizabeth A. Jones [a], J. Michael Wright [b,*], Glenn Rice [b], Brian T. Buckley [c], Melina S. Magsumbol [e], Dana B. Barr [d], Bryan L. Williams [e]

[a] Association of Schools of Public Health, Washington DC 20005, USA
[b] Environmental Protection Agency, National Center for Environmental Assessment, Cincinnati, OH 45268, USA
[c] Environmental and Occupational Health Sciences Institute, Rutgers University, Piscataway, NJ 08854, USA
[d] Rollins School of Public Health of Emory University, Atlanta, GA 30322, USA
[e] Georgia State University, College of Education, Atlanta, GA 30303, USA

ARTICLE INFO

Article history:
Received 24 June 2009
Accepted 12 April 2010

Keywords:
Lead
Metals
Pregnancy
Environmental epidemiology
Urban health

ABSTRACT

Objectives: We measured concentrations of lead (Pb), manganese (Mn), chromium (Cr), and copper (Cu) in umbilical cord whole blood and examined sources of environmental Pb exposures in a predominantly African-American population.
Methods: Between April and July 2006, we collected reproductive histories, questionnaires, and blood samples from 102 women, aged 16–45 years, who delivered at a Memphis, TN hospital.
Results: The prevalence of preeclampsia and low birth weight infancy in the study population was 11% and 10%, respectively. Twenty-eight percent of mothers reported living near a potential Pb-contaminated area, while 43% lived in a residence built before 1978. Geometric mean (GM) concentrations for umbilical cord blood in the study population were 1.3, 3.5, 9.0, and 52.0 µg/dL for Pb, Mn, Cr, and Cu, respectively. Six neonates had cord blood Pb (CBL) concentrations above 10 µg/dL, while 20 had CBL concentrations ≥2 µg/dL. GM umbilical CBL levels were higher in neonates born to women living near a potential Pb-contaminated area (2.2 vs. 1.1 µg/dL) and those with friends, family or household members exposed to lead products (1.6 vs. 1.1 µg/dL). Some evidence of an exposure–response relationship was also detected between all four metal concentrations and an increasing number of maternal lead exposures. After adjustment for confounding, proximity to a Pb-contaminated area was the strongest environmental determinant of CBL levels among neonates with CBL concentrations of ≥2 µg/dL (odds ratio = 5.1; 95% CI = 1.6, 16.7).
Conclusions: Metal concentrations were elevated in this population, and CBL levels were associated with proximity to Pb-contaminated areas.

Published by Elsevier Ltd.

1. Introduction

Many metals accumulate in soft tissue and bone over time and can influence the toxicokinetics of other metals and trace elements in the body. Some metals, such as Cr and Mn, are essential nutrients and primary exposure occurs through diet. Less frequently, environmental and occupational sources contribute to these metal exposures. Metals including lead (Pb), mercury, manganese (Mn), chromium (Cr), copper (Cu) and cadmium (Cd) are neurological, renal, and developmental toxicants at certain concentrations (ATSDR, 2004). There is some uncertainty, however, as to the human health impact related to low level exposures to these metals. Additionally, there is limited knowledge regarding the cumulative effects of metal mixtures in humans, however additive cardiovascular, neurological, and testicular effects have been detected in animals (Hu et al., 2008).

Fetal development is one of the most sensitive life stages for endogenous and exogenous insults primarily due to rapid cell division and apoptosis, morphogenesis, and cellular differentiation. Furthermore, developing fetuses are especially vulnerable to *in utero* exposures to metals and other transplacental contaminants because of limited renal and biliary elimination and the inability to metabolize toxicants readily (Raghunath et al., 2000; Ziaee et al., 2007; Smargiassi et al., 2002).

Additionally, Pb that accumulates in bone throughout a woman's lifetime has the potential to enter the bloodstream when it is mobilized during pregnancy (Gulson et al., 2003). This Pb mobilization is influenced by the same mechanisms that mobilize calcium during the third trimester of pregnancy (i.e., release of parathyroid hormone and increased intestinal absorption and bone resorption) (Rothenberg et al., 1994). Although the transfer of Pb from mother to fetus is only partially understood (Hu et al., 2006), maternal blood Pb concentrations are highly correlated ($r = 0.44$–0.79) with umbilical cord blood Pb (CBL) levels (Raghunath et al., 2000; Schell et al., 2003; Ong et al., 1993; Dietrich et al., 1987; Lauwerys et al., 1978). Maternal and

* Corresponding author. 26 W. Martin Luther King Dr. MS-A110, Cincinnati, OH 45268, USA. Tel.: +1 513 569 7922; fax: +1 513 487 2539.
E-mail address: Wright.Michael@epa.gov (J.M. Wright).

0160-4120/$ – see front matter. Published by Elsevier Ltd.
doi:10.1016/j.envint.2010.04.007

umbilical cord blood concentrations also are correlated for Cd (r = 0.38–0.81), Cu (r = 0.34–0.58), and other essential metals that are largely influenced by dietary sources, such as iron (Fe; r = 0.81), zinc (Zn; r = 0.78), and magnesium (r = 0.78) (Raghunath et al., 2000; Ong et al., 1993; Salpietro et al., 2002; Lauwerys et al., 1978).

In addition to the inherent susceptibility of developing fetuses to metal exposures, maternal and familial factors (e.g., lifestyle and socioeconomic status) may make the fetus even more vulnerable to various environmental insults (Matthews and Meaney, 2005). We examined maternal residential and environmental exposures as well as lifestyle factors in relation to umbilical cord blood Pb, Mn, Cr, and Cu concentrations in a predominantly urban African-American population.

2. Methods

2.1. Study population

Between April and July 2006, we recruited 102 women prior to delivery, aged 16–45 years, who delivered a live birth at the Regional Medical Center of Memphis Rout Center for Women and Newborns. We excluded women who gave birth prior to 27 weeks of gestation; resided for less than 5 months in Shelby County, TN during their pregnancy; experienced multiple gestational pregnancies; or had diabetes, hepatitis, or a history of endocrine, renal, collagen, pulmonary or heart disease. The study protocol used by the University of Tennessee Health Science Center's Department of Pediatrics was approved by the Institutional Review Board.

2.2. Maternal interview

We conducted interviews one to two days after delivery with the mothers to gather information about personal, household, and environmental exposure to metals. We asked specific questions pertaining to pregnancy and home residency (i.e., residence constructed prior to 1978) as well as exposures to paint via recent household remodeling. We also asked questions about living near hazardous waste sites, heavily traveled highways, car repair shops, and construction sites during pregnancy. After obtaining informed consent, we collected maternal and birth data from medical center worksheets and birth certificates. Self-reported race/ethnicity classification included African-American, Caucasian, Asian, Native American, Hispanic, or Other. Given the small numbers of non-African-American participants (n = 12), we combined those reporting Caucasian, Asian or Hispanic race/ethnicity into the Other category for comparison with the African-American population. The Kotelchuck Adequacy of Prenatal Care Utilization Index, a measure integrating the number of prenatal care visits from initiation to delivery, gestational age, and the month prenatal care began, was used to evaluate the adequacy of each participant's prenatal care (Kotelchuck, 1994).

2.3. Umbilical cord whole blood collection and analysis

After obtaining informed consent, we collected 30–50 mL umbilical cord blood samples from the study participants and collected maternal and birth data from medical center worksheets and birth certificates. For the analysis of Cr, Cu, Mn, and Pb, cord blood was transferred to 7-mL vacutainers with K_3EDTA anticoagulant and placed into cold-storage (0 °C) until shipped for analysis at Rutgers University's Environmental and Occupational Health Sciences Institute. We quantified cord blood metal concentrations using inductively coupled plasma mass spectrometry on a Thermo-elemental X5 spectrophotometer (Thermo Fisher Scientific, Waltham, MA). The samples were digested in concentrated nitric acid using a microwave sample digester, CEM Mars X5 (CEM Corporation, Mathews, NC) and were diluted to a final acid concentration of approximately 5%. Standard solutions were prepared in 5% nitric acid. Sample masses were scanned from lithium through uranium for semi-quantitative analysis. A suite of 24 elements were quantified against standard curves within this mass range. An average concentration calculated from multiple isotopes was reported for elements such as Pb. Concentrations equal to limit of detection divided by square root of two were substituted for non detects for the four metals that were analyzed. Statistical analyses were not conducted on metals with mostly (>80%) non detects; measures of central tendency and variability are provided for an additional seven metals with less than 50% non detects (see Supplemental Table 1).

Standard laboratory quality assurance/quality control protocols were maintained throughout the extraction and analysis processes. Differences among the averaged concentrations were always less than a 3% relative standard deviation. Quality control samples (NIST AB custom mix, High Purity Standards) were analyzed before and after each sample set with recoveries between 80 and 120% as the acceptance criteria for a sample run. Sample blanks were created using nitric acid and deionized water. Blanks were microwaved during each sample run and evaluated for laboratory contamination. The limit of detection ranged from 0.1 to 0.5 ng metal/mL for the diluted samples and was dependent on the amount of sample used and the element analyzed. This method has previously been used for metals analysis in human serum (Xie et al., 2007) and whole blood samples (Riedt et al., 2009).

2.4. Statistical analysis

We used SAS version 9.1 for the statistical analysis. Since the cord blood metal concentrations were not normally distributed (e.g., skewness for Pb = 4.0), a logarithmic transformation was used to normalize the distribution for parametric analysis. We conducted analyses of geometric mean (GM) metal concentrations stratified by maternal and neonatal characteristics. We examined exposure–response relationships by creating aggregate maternal lead exposure categories. We examined Spearman correlation coefficients and used logistic regression to identify maternal and neonatal predictors of elevated CBL levels (defined as ≥2 µg/dL). We retained potential confounding variables in the multivariate regression models if their inclusion resulted in at least a 10% change (Rothman and Greenland, 1998) in the odds ratio (OR) compared to the blood Pb and Pb-contaminated area (i.e., unadjusted) model. Statistical significance was determined using a p-value of <0.05, and precision was assessed via examination of 95% confidence intervals (CIs).

3. Results

The GM CBL concentration was 1.3 µg/dL, and the arithmetic mean in the study population was 2.4 µg/dL (Table 1). The GMs for Mn, Cr, and Cu were 3.5, 9.0, and 52.0 µg/dL, while the arithmetic means were 4.4, 10.0, and 54.3 µg/dL, respectively. Spearman correlation coefficients for Pb, Mn, Cr, and Cu ranged from 0.14 to 0.62 with stronger correlations detected between metals that were most likely to be influenced by mother's nutritional status (i.e., intake of Mn, Cr, and Cu). Six neonates in this population had CBL levels exceeding the Centers for Disease Control and Prevention (CDC)'s level of concern of 10 µg/dL and 20 neonates had CBL concentrations ≥2 µg/dL.

Table 1
Umbilical cord metal concentrations (µg/dL) for other metals analyzed among 102 study subjects.

Metal	GM	AM	Median	SD	Q1	Q3	r-Pb	r-Mn	r-Cr
Pb	1.3	2.4	0.85	4.3	0.7	1.2	–	–	–
Mn	3.5	4.4	3.0	3.5	2.2	5.7	0.24[a]	–	–
Cr	9.0	10.0	9.4	5.0	7.6	11.3	0.25[a]	0.57[a]	–
Cu	52.0	54.3	50.6	16.5	43.9	64.1	0.14	0.62[a]	0.48[a]

GM = geometric mean, AM = arithmetic mean, SD = standard deviation, Q1 = 25th percentile, Q3 = 75th percentile, r = Spearman's correlation coefficient, Pb = lead, Mn = manganese, Cr = chromium, Cu = copper.

[a] p-values<0.05 for Spearman's correlation coefficients.