SHORT COMMUNICATION

Selenium in placenta predicts birth weight in normal but not intrauterine growth restriction pregnancy

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Abstract

Placental selenium, lead and cadmium concentrations were determined in a group of pregnancies with birth weight appropriate for gestational age and in a group of intrauterine growth restriction cases. Following adjustment for a number of confounding variables, selenium was found to be a significant predictor of newborn weight only in the group of pregnancies with birth weights appropriate for gestational age. Placental lead and cadmium levels were not associated with birth weight in either group.
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Keywords: Selenium; Birth weight; Eastern Croatia

Introduction

Essentiality of selenium (Se) implies a range of important functions in the human body, primarily thyroid hormone metabolism and antioxidant action of several selenoproteins [1]. Deficient and low status of the element has been connected with a number of disorders including adverse pregnancy outcomes, e.g. preterm deliveries [2], miscarriages [3,4] and preeclampsia [5]. Placental cadmium (Cd) and lead (Pb) were found to be inversely associated with birth weight [6–8], and they interact with Se in the body whereby Se can reduce their toxic effects [9,10]. Se intake and food levels seem to be suboptimal in eastern Croatia [11,12]. Since placenta is considered a good biomarker of Se provision as well as of exposure to toxic elements [13,14], this pilot study examined whether the placental levels of Se, Cd and Pb were related to fetal growth.

Materials and methods

Collection of placenta samples was performed during 2003 and 2004 at the Osijek Clinical Hospital from healthy mother–newborn pairs. Intrauterine growth restriction was defined as birth weight below the 10th percentile at gestational age according to data reported by Dražančić et al. [15]. All IUGR cases ($n = 57$) were sampled and women agreed to take part in the study. Normal pregnancies ($n = 44$) were sampled randomly and all women gave informed consent. Smokers as well as women with abnormalities during pregnancy (preeclampsia, impaired glucose tolerance, diabetes) were excluded. Additionally, several samples and/or questionnaires were misplaced and a few participants were

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excluded due to incomplete data. Following exclusions, 85 of 107 initial samples were further processed; 49 IUGR cases and 36 births with birth weights appropriate for gestational age. The share of preterm deliveries (<37 week) in the group appropriate for gestational age (3/36, i.e. 8.3%) was similar to the mean incidence of preterm deliveries for the years 2004–2006 (9.8%) at the Department of Obstetrics and Gynaecology, Osijek Clinical Hospital. Characteristics of mothers and newborns (obtained from women and delivery records) are given in Table 1. The high end of the range of birth weights for the IUGR infants (3020 g) and the low end of the range of birth weights for the infants with birth weights appropriate for gestational age (1200 g) reflect the combination of the length of gestation and newborn sex of these multiparous subjects (39.9 weeks and male in the former case, and 29.3 weeks and female in the latter). A total of 56 infants had a birth weight higher or equal to 2500 g; 22 infants in the IUGR group (2723.2 ± 144.2 g) and 34 in the 'normal' group (3537.1 ± 418.7 g); 29 infants had birth weight below 2500 g; of these, 27 were IUGR cases (2118.9 ± 435.0 g) and two infants in the group appropriate for gestational age had birth weight below 2500 g (1450.0 ± 353.6 g).

Placentas were collected immediately after delivery and stored in polyethylene bags at −20 °C until further processing. Following removal of connective tissue, placental samples were cut by 'cake section', thawed and several small portions combined for digestion. Approximately 3 g was transferred to borosilicate tubes together with 5 mL concentrated suprapure nitric acid, 1 mL concentrated sulfuric acid and 1 mL 70% perchloric acid. The mixture was left overnight for predigestion. Wet digestion was performed in a heated block with air cooling and reflux. The temperature was gradually raised until solutions cleared, and kept at 195–205 °C until white fumes appeared. Total Se in digestates was determined using hydride generation atomic absorption spectrometry (Perkin-Elmer 2380, MHS Type 10) with 3% NaBH4 in 1% NaOH following

the reduction of Se (VI) to Se (IV) in digestates according to procedure described earlier [12]. One gram of placenta samples used for Cd and Pb determination was digested using 10 mL concentrated suprapur nitric acid in a microwave digestion oven (CEM, MDS 2000) and the elemental content was measured in a graphite furnace atomic absorption spectrometer (AAnalyst 600, Perkin-Elmer). All analyses were performed at least in duplicate. Calibration was performed by the method of standard additions. Accuracy of elemental analysis was checked using reference material (DORM-2, Dogfish muscle, National Research Council Canada) containing 1.40 ± 0.09 µg/g total Se, 0.043 ± 0.008 µg/g Cd and 0.065 ± 0.007 µg/g Pb and the determined concentrations were 1.33 ± 0.02, 0.050 ± 0.0008 and 0.062 ± 0.005 µg/g, respectively. Detection limits were 0.2 µg/L for Se, 0.03 µg/L for Cd and 0.2 µg/L for Pb.

The data sets were tested for normality of distribution (Shapiro–Wilk's W test), group means or medians were calculated and the difference was examined using Mann–Whitney U test or a t-test. Spearman's rank and Pearson's product-moment partial correlations between variables were estimated. Univariate regression analysis was performed to examine the contribution of various variables to birth weight. Selected variables were then included in the stepwise least-squares multiple regression analysis. Variable was considered in the stepwise multiple regression analysis when the 95% confidence interval (CI) of the regression coefficient in the univariate regressions did not include zero. Software programs Statistica 7.0 (StatSoft), SPSS 15.0 (SPSS) and Microsoft Office Excel 2003 (Microsoft) were used for these purposes.

Results

Determined levels of elements in placenta are given in Table 2. The Se content was higher in the 'normal' group, while Pb and Cd levels were higher in the IUGR

Table 1. Maternal and newborn characteristics

	IUGR ($n = 49$)	AGA ($n = 36$)	Total ($n = 85$)
Gestation (week)	38.6 (28.6–40.9)	39.9 (29.3–40.6)	39.6 (28.6–40.9)
Mother's BMI (kg/m^2)	25.1 (19.1–39.0)	27.3 (18.7–38.4)	26.1 (18.7–39.0)
Mother's age (yr)	26.0 ± 4.7	27.5 ± 5.8	26.6 ± 5.2
Residence (% urban)	42.9	58.3	49.4
Education (% university)	6.1	8.3	7.1
Number of deliveries	0.78 ± 0.98	0.64 ± 0.68	0.72 ± 0.87
Male/female ratio	1.13	1.40	1.23
Primipara/multipara ratio	0.96	0.80	0.89
Newborn weight (g)	2390 (800–3020)	3421 (1200–4320)	2760 (800–4320)
Newborn length (cm)	46.4 ± 1.8	50.2 ± 2.3	48.1 ± 2.8

IUGR – intrauterine growth restriction pregnancy; AGA – birth weights appropriate for gestational age.
Mean ± SD or median (range).