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Elemental analysis of serum and hair from pre-eclamptic South African women

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ABSTRACT

Pre-eclampsia is a hypertensive disorder that is associated with adverse maternal and perinatal outcomes. It has been proposed that specific trace and macro elements associated with antioxidant activities may also play a contributory role in aetiology of pre-eclampsia. The aim of this study was to measure the concentrations of thirteen different elements in hair and serum samples from women with a diagnosis of pre-eclampsia and compare them with normotensive controls. Venous blood and pubic hair samples were collected from forty-three pre-eclamptic and twenty-three normotensive pregnant women. In each sample, the concentration of arsenic (As); calcium (Ca); cadmium (Cd); chromium (Cr); cobalt (Co); magnesium (Mg); manganese (Mn); iron (Fe); copper (Cu); lead (Pb); selenium (Se); nickel (Ni); zinc (Zn) were measured using inductively coupled plasma-optical emission spectrometry. Cobalt concentration in hair was significantly lower in the pre-eclampsia group (1.56 ± 0.74 μg/g) compared to the normotensive group (2.89 ± 4.99 μg/g) ($p = 0.02$). The concentrations of Zn and Cr were significantly higher in hair samples from the pre-eclamptic group, compared to the normotensive control group (Zn, 395.99 ± 48.60 vs 330.88 ± 29.70 μg/g; Cr, 13.31 ± 2.67 vs 11.05 ± 7.62 μg/g: $p \leq 0.05$). There were no significant differences in the hair levels of other elements between groups. Serum Zn was significantly higher in the pre-eclamptic group (0.16–253.4 mg/L) compared to the normotensive group (0.2–48.4 mg/L) ($p = 0.01$). Serum Ca, Co, Cu, Mg, Mn and Se levels were found to be significantly lower in the pre-eclamptic group compared to the normotensive group ($p < 0.05$). This study confirms the association between pre-eclampsia and maternal trace as well as macro element levels.

1. Introduction

The nutritional status of women of reproductive age and during pregnancy is important for their own health and healthy birth outcomes [1,2]. It is well documented that pregnancy is the time during which increased nutrients are most needed by the mother to support fetal growth and development while maintaining maternal homeostasis and preparing the mother for lactation [3]. It is also a period of small, continuous gestation-related physiologic changes that affect the metabolism of all nutrients. For instance, within several weeks of conception an endocrine organ (placenta) is formed which secretes hormones that impacts the metabolism of all nutrients [3]. Thereafter, the fetus is dependent on the mother to deliver its nutrients via the placenta. Since the placenta carries oxygenated, nutrient-rich blood to the fetus, it is considered to be rich in micronutrient-requiring antioxidant enzymes. These include glutathione peroxidases (selenium) and superoxide dismutases (copper, zinc and manganese), which are vital for protecting the embryo and placenta from oxidative stress. Inadequate antioxidant activity has been postulated to be related to reduction in placental vascularization and blood supply to the fetus. This may potentially result in hypoxia and ischaemia, and is likely to contribute to pre-eclampsia and poor fetal growth [4]. Therefore, deficiencies of macronutrients or micronutrients can increase a women's risk for pregnancy complications such as pre-eclampsia [5].

Pre-eclampsia is a multi-systemic condition occurring after 20 weeks of gestation. It is clinically characterised by new onset hypertension (systolic blood pressure ≥140 mmHg; diastolic blood

Abbreviations: As, arsenic; Ca, calcium; Cd, cadmium; Cr, chromium; Co, cobalt; Mg, magnesium; Mn, manganese; Fe, iron; Cu, copper; Pb, lead; Se, selenium; Ni, nickel; Zn, zinc.

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pressure ≥90 mmHg) and proteinuria (≥300 mg/24 h) [6]. Globally, pre-eclampsia is one of the major causes of maternal and neonatal morbidity and mortality. In South Africa, pre-eclampsia is also the commonest direct cause of maternal deaths [7]. Despite continuing research, the pathogenesis of this disorder is still unclear and delivery of the placenta remains the only cure [6]. Presently, a large number of other studies suggest that nutritional factors may also play a major role in blood pressure regulation, cardiovascular disease, hypertension and pre-eclampsia development [8–10].

Magnesium (Mg) and calcium (Ca) deficiency has been implicated as a possible cause of pre-eclampsia [11] since its supplementation during pregnancy may reduce the incidence of high blood pressure, pre-eclampsia, low birth weight and pre-term birth [12]. In addition, iron (Fe) supplements and increased Fe stores in the third trimester are associated with increased oxidative stress and the risk of pre-eclampsia development [13]. Other trace element deficiencies such as zinc (Zn), copper (Cu) and selenium (Se) have been related to various reproductive problems (e.g. infertility, placental abruption, premature rupture of membranes, stillbirths and low birth weight) including pre-eclampsia [14]. A number of studies have reported on the implication of toxic metals such as lead Pb and cadmium (Cd) in pre-eclampsia. Human exposure to excess toxic metals in the environment and a deficiency of bio-elements essential for antioxidant defense mechanisms causes oxidative stress, which leads to pre-eclampsia [15–18]. However, further epidemiological and clinical studies utilizing diverse biological samples in defined populations may help understand the role of various essential and toxic metals in pre-eclampsia. Therefore, the aim of this study was to evaluate the concentrations of thirteen different elements in hair and serum samples from women with a diagnosis of pre-eclampsia.

2. Material and methods

2.1. Study design

Institutional ethics approval (BE092/16) was granted by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal and informed consent was obtained from all women. This study was conducted in a large urban regional hospital. The study population consisted of normotensive (n = 23) and pre-eclamptic (n = 43) women. Clinical and demographic data were recorded by a research nurse.

2.2. Hair and serum sample collection

Hair and serum samples were collected from the same women for each study group. Hair samples were collected from the pubic area by using a sterile shaving razor and stored in sterile plastic bags at room temperature. Blood was drawn from the ante-cubital vein and centrifuged for 10 min at 3000 rpm to extract serum.

2.3. Digestion of hair and serum samples

For instrumental analysis, human biological samples such as serum and hair require an additional digestion step to destroy the organic matrix. This promotes the long-term stability of the ICP as digested samples prevent build-up of salt and carbon deposits on the cones of the instrument, reduces spectral and non-spectral interferences, improves the overall throughput of the method and allows for the analysis of larger sample sizes.

The samples of pubic hair were rinsed with distilled water and thoroughly dried with blotting paper before digestion. To each sample (0.01 g of hair or 0.5 mL of serum), 10 mL of 70% nitric acid was added and heated until complete digestion occurred. Thereafter, digests were diluted aqueously in a 25 mL volumetric flask. Three and two replicates were prepared for serum and hair samples, respectively. Digests were analysed in triplicate. In order to eliminate matrix effects, calibration was by use of external standards that matched the matrix of the samples. Reagent blanks were prepared by addition of double distilled water to nitric acid (same volume as the samples). For method validation, the certified reference material (CRM), lyophilised serum control for trace elements (Ref No: 8880; ClinChek®, Munich, Germany), was used and was reconstituted as per instruction manual and digested under the same conditions as the samples. All samples were transferred into polytetrafluoroethylene (PTFE) bottles and stored in the refrigerator until elemental analysis. Elemental standards (1000 ppm) of analytical-reagent grade were purchased from Sigma Aldrich (St Louis, MO, USA). Working standards were prepared using double distilled water and 10 mL of 70% nitric acid to match the sample matrix.

2.4. Elemental analysis of samples

Elemental analysis of digested hair and serum samples were conducted by inductively coupled plasma-optical emission spectrometry (ICP-OES, Optima™ 5300 DV) at different wavelengths for each of the analytes. Wavelength selection was based on minimum spectral interferences and the wavelengths selected were: As (197 nm), Ca (393 nm), Cd (227 nm), Co (231 nm), Cr (268 nm), Cu (325 nm), Fe (260 nm), Mg (280 nm), Mn (261 nm), Ni (232 nm), Pb (220 nm), Se (196 nm) and Zn (214 nm). The instrument detection limits for each analyte was As (4.29 ppb), Cd (0.607 ppb), Co (0.346 ppb), Cr (0.744 ppb), Cu (1.41 ppb), Mn (0.095 nm), Ni (0.839 ppb), Pb (2.21 ppb) and Se (2.54 ppb).

2.5. Statistical analysis

The Statistical package for the Social Sciences (PASW Statistics 23, IBM Corporation, Cornell, New York) was used for statistical analyses. Parametric data was expressed as mean ± standard deviation and non-parametric data expressed as median ± SEM. Statistical significance of the data was determined using Independent T-test and Mann-Whitney. Pearson correlation coefficient was used to find the relationship among various study parameters. A p-value ≤ 0.05 was considered statistically significant.

3. Results

3.1. Quality assurance

The experimental values obtained for the CRM (n = 6, p = 0.05) were (in μg/L) 4.57, 7.37, 3.85, 10.42, 61.97, 796.8, 1334, 12382, 1345 for Cd, Cr, Mn, Ni, Se, Cu, Fe, Mg and Zn; compared to certified value ranges (in μg/L) (3.63–5.45), (5.99–8.99), (3.81–5.71), (7.08–10.6), (52.9–79.3), (681–921), (1330–1790), (11200–13600) and (1120–1520). Experimental values agreed well with certified values thereby validating the method.

3.2. Clinical and demographic data

The clinical and socio-demographic parameters of the study population are summarized in Table 1. The mean maternal age, weight and body mass index (BMI) of the pre-eclamptic group were not significantly different from those of the normotensive group (p > 0.05). There were significant differences between the groups for mean diastolic blood pressure (p = 0.0001), systolic blood pressure (p = 0.0001), proteinuria (p = 0.0001) and gestational age (p = 0.004). There was a statistically significant lower rate of delivery by elective cesarean delivery in the normotensive (22%) group compared to the pre-eclamptic (47%) group (p = 0.05), with normal

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