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Metal/metalloid levels in urine and seminal plasma in relation to computer-aided sperm analysis motion parameters

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HIGHLIGHTS

- Urinary and seminal plasma metals were determined among 746 Chinese men.
- Six computer-aided sperm analysis (CASA) motion parameters were also determined.
- Seminal plasma As, Se, Mn and Zn were inversely associated with CASA motion parameter.
- No convincing association was found between urinary metals and CASA motion parameters.
- Urinary metal concentrations poorly predicted the exposure levels in seminal plasma.

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ABSTRACT

Background: Exposure to high levels of metals/metalloids may impair semen quality. Computer-aided sperm analysis (CASA) can be used for kinematic analysis of spermatozoa, which provides additional insights into sperm motion characteristics.
Objective: To explore the associations of urinary and seminal plasma metal/metalloid concentrations with CASA motion parameters and assess the degree of correspondence between the two sample types.
Methods: Eighteen metals/metalloids in seminal plasma and repeated urine samples were determined among 746 men recruited from a reproductive center. We assessed their associations with 6 CASA motion parameters [i.e., straight-line velocity (VSL), curvilinear velocity (VCL), average path velocity (VAP), linearity (LIN), straightness (STR) and amplitude head displacement (ALH)] using multivariable linear regression models.
Results: We found significantly inverse dose-dependent relationships between seminal plasma arsenic (As) and VSL, VCL and VAP, between seminal plasma selenium (Se) and VSL and VAP, between seminal plasma zinc (Zn) and STR and LIN, and between seminal plasma manganese (Mn) and LIN in single-metal models [all false discovery rate (FDR) adjusted P for trend < 0.05]. These dose-response relationships remained statistically significant based on multiple-metal models and restricted cubic spline functions. Metal/metalloid concentrations in urine poorly predicted the same-day seminal plasma concentrations [coefficient of determination (R^2) < 0.15]. We didn't find any significant associations between urinary metal/metalloid concentrations and the CASA motion parameters.

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Conclusion: Exposure to high levels of As, Se, Mn and Zn may impair sperm motion capacity. Concentrations of metals/metalloids in spot urine samples cannot accurately predict same-day seminal plasma exposure levels.

1. Introduction

Evidence of falling semen quality has been reported in many studies (Carlsen et al., 1992; Levine et al., 2017; Swan et al., 2000), which becomes a serious public health concern. Many animal and human studies suggest that exposure to metals/metalloids (hereafter, simply referred to as "metals"), may partly contribute to this decline. Metals are distributed broadly in the environment because of original existence in nature and emissions from human activities. Humans can be exposed to metals either voluntarily through supplementation, or involuntarily through intake of contaminated environmental media (e.g., food, water). Aluminum (Al), arsenic (As), cadmium (Cd), antimony (Sb), thallium (Tl), lead (Pb) and uranium (U) are nonessential xenobiotics. Human and animal evidence suggests that these metals may adversely affect male reproductive health at relatively low levels (Kasperczyk et al., 2008; Li et al., 2016; Marzec-Wroblewska et al., 2012; Souidi et al., 2009; Wang et al., 2016d, 2017; Wu et al., 2012). Other metals, such as chromium (Cr), copper (Cu), iron (Fe), manganese (Mn), zinc (Zn), selenium (Se) and molybdenum (Mo), are essential for certain physiological functions (Kasperczyk et al., 2016a; Skandhan et al., 2012; Tajaddini et al., 2014; Zeng et al., 2015). However, excessive exposure may also impair male reproductive health (Jeng et al., 2015; Kasperczyk et al., 2016b; Li et al., 2012a; Marzec-Wroblewska et al., 2012; McGough and Jardine, 2017; Wang et al., 2016a, 2016b).

Computer-aided sperm analysis (CASA) parameters, including straight-line velocity (VSL), curvilinear velocity (VCL), average path velocity (VAP), linearity (LIN), straightness (STR) and amplitude head displacement (ALH), are best used for kinematic analysis of spermatozoa, which provide additional insights into sperm motion characteristics (Alipour et al., 2017; Goodson et al., 2017). Both in vitro and in vivo studies have demonstrated that CASA motion characteristics of progressively motile spermatozoa are closely related to fertilization rates and time to conception (Barratt et al., 1993; Donnelly et al., 1998; Garrett et al., 2003; Irvine et al., 1994; Krause, 1995; Larsen et al., 2000; Liu et al., 1991; Shibahara et al., 2004). Several researchers explored the effects of exposure to certain chemicals (e.g., epichlorohydrin and alpha-chlorohydrin) on CASA motion parameters in animal models and revealed that the CASA characteristics were more sensitive markers of reproductive toxicity than conventional sperm quality parameters (Perreault and Cancel, 2001; Slott et al., 1995, 1997). However, no human studies to date have evaluated the associations between metal exposure and CASA motion parameters.

Concentrations of metals in urine are frequently used as exposure biomarkers in population studies. However, our variability analysis revealed that urinary metal concentrations varied greatly over a 3-month period and that single measurement could result in a moderate degree of exposure misclassification; collection of repeated samples from each subject improved the classification (Wang et al., 2016c). Besides, metals in seminal plasma are suspected as more direct makers for the exposure status of male reproductive system than that in urine, and seminal plasma Al, As, Mn, Co, Ni, Se, Cu, Zn, Mo, Cd, Sn and Pb have been tested for their exposure effects on male reproductive disorders in previous studies (Guzikowski et al., 2015; Wang et al., 2017; Wu et al., 2012; Zafar et al., 2015). Therefore, in this study we simultaneously determined concentrations of 18 metals both in seminal plasma and repeated urine samples among 746 Chinese adult men with aims to: ***a***) explore the associations of urinary and seminal plasma metals with CASA motion parameters; and ***b***) assess the degree of correspondence between these two sample types.

2. Materials and methods

2.1. Participants and sample collection

This study was approved by the Ethics Committee of the Tongji Medical College. Our eligible participants were men of reproductive age (18–55 years) who came to the Reproductive Center of Tongji Hospital for semen examination (Wang et al., 2015). From March to June 2013, 1490 men without knowledge of their fertility status were recruited. Each enrollee was asked to sign an informed consent and complete a questionnaire covering information about their lifestyle habits, occupational exposure, health condition and the history of having ever fathered a pregnancy. The participants were also asked to provide two spot urine samples at different times of their visiting day (at least 2 h apart) and donate a semen sample in a private room (Wang et al., 2016d). We excluded 450 men who had self-reported diseases that are related to male reproductive disorders (e.g., epididymitis, undescended testicle, vasectomy, varicocele and hernia repair), or other health problems that affect metal excretions (e.g., diabetes and adrenal disorder). We also ruled out 294 participants who didn't offer enough seminal plasma for metal determinations. A total of 746 participants were eventually remained in our present study.

2.2. Metals analysis

The 18 metals (Al, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Mo, Cd, Sn, Sb, W, Tl, Pb and U) in urine and seminal plasma were analyzed using an inductively coupled plasma-mass spectrometer, which has been described in details in our prior studies (Wang et al., 2016d, 2017). Briefly, for sample treatment, a 3.0-mL aliquot of urine was acidified with 15 μL of 67% HNO_3 (v/v; OptimaTM grade, Fisher Scientific, Fair Lawn, NJ, USA) at 5 °C for at least 24 h, then 1.0 mL of each urine sample was diluted to 5.0 mL using 1.2% HNO_3 (v/v; OptimaTM grade, Fisher). For seminal plasma, 0.4 mL of seminal plasma was transferred to a trace element-free polyethylene tube and then diluted to 4 mL with 1.2% HNO_3 (v/v; OptimaTM grade, Fisher); we stored the samples in a freezer overnight at 5 °C. Our measurements of the standard reference materials (SRM) 2670a and SRM 1640a, and the certified reference materials ClinChek no. 8883 and 8884 were within the range of the reference values. Spiked recoveries of metal concentrations in pooled urine and seminal plasma samples were 82%–117% and 82%–114%, respectively. The limits of quantification (LOQ) of these metals in urine and seminal plasma were in a range of 0.0013–0.29 $\mu g\,L^{-1}$ and 0.0026–0.49 $\mu g\,L^{-1}$, respectively. Values below the LOQ were assigned as $LOQ/\sqrt{2}$ for data analysis. An automated clinical chemistry analyzer was used to measure concentrations of urinary