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Concentrations of vanadium in urine and seminal plasma in relation to semen quality parameters, spermatozoa DNA damage and serum hormone levels

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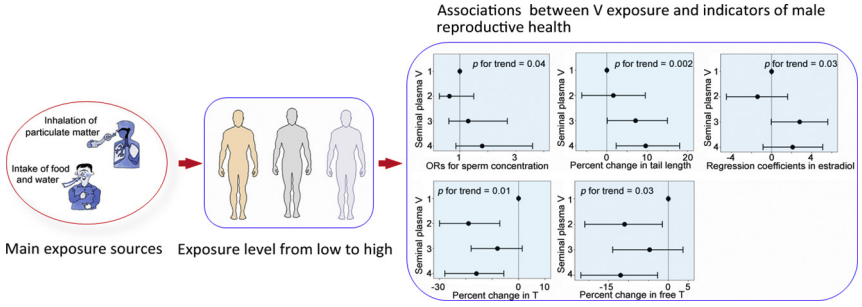
HIGHLIGHTS

- Both urinary and seminal plasma vanadium (V) were determined in 746 men.
- Seminal plasma V was associated with increased tail length and serum estradiol.
- Inverse relationships were observed for seminal plasma V with total T and free T.
- V was associated with increasing ORs for the below-reference sperm concentration.

GRAPHICAL ABSTRACT



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ABSTRACT

Widespread human exposure to vanadium has been well documented. Vanadium exposure was reported to induce male reproductive toxicity in toxicological studies, yet human epidemiologic studies are lacking. Here we determined the associations between environmental exposure to vanadium and semen quality, spermatozoa DNA damage and serum reproductive hormones. Concentrations of vanadium in seminal plasma and repeated urine samples were determined among 764 men recruited from a reproductive medicine centre. Associations of vanadium concentrations with semen quality parameters ($n = 764$), DNA integrity measures ($n = 404$) and serum reproductive hormones ($n = 381$) were assessed by logistic or linear regression models with adjustment for potential confounders. Significant positive dose–response relationships were observed between vanadium concentrations in seminal plasma and tail length and serum estradiol, as well as odds ratios for a below-reference-value sperm concentration; whereas inverse relationships between seminal plasma vanadium with total testosterone (T) and free T (all p values for trends <0.05) were observed. These relationships were maintained after adjusting for seminal plasma concentrations of other elements (i.e., arsenic, cadmium, copper, selenium, or tin). No significant associations was revealed between urinary vanadium concentrations and semen

Abbreviations: FSH, follicle-stimulating hormone; LH, luteinizing hormone; LOQ, the limits of quantification; SHBG, sex hormone-binding globulin; T, testosterone; VIF, variance inflation factor.

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quality, spermatozoa DNA integrity and reproductive hormones. Our findings suggested that elevated vanadium exposure may be adversely associated with male reproductive health, and that seminal plasma vanadium may be a more direct exposure biomarker for the male reproductive system than urinary vanadium.

1. Introduction

Vanadium is a transition metal that is ubiquitously present in the soil, water and the atmosphere due to both natural processes and anthropogenic activities (e.g., industry, mining, combustion of fossil fuels, recycling of domestic waste and application of fertilizer and pesticide) (Imtiaz et al., 2015; Yang et al., 2017). It is estimated that approximately 2.3×10^5 tons of vanadium are introduced to the environment annually (Hope, 1997). China is the world's largest vanadium-producing country, accounting for about 57% of the global vanadium production (GCVIR, 2014). As a result, 26.5% of soils, mainly scattered in southwestern China, are contaminated by vanadium (Yang et al., 2017). The general population are primarily exposed to vanadium through intake of contaminated food and drinking water (Fortoul et al., 2014), and through inhalation of suspended particulate matter (Moreno et al., 2010; Riediker et al., 2003).

Vanadium is probably an essential trace element for humans and its tolerable upper intake level has been recommended as 1.8 mg/day (IOM, 2001). However, excessive exposure can cause adverse effects on the physiology and morphology of tissues both in animals and humans, including male reproductive system (Wilk et al., 2017). Animal studies have shown that vanadium exposure induces male reproductive toxicity by producing excessive oxidative stress (Chandra et al., 2007c), manifested as decreased testicular weight (Chandra et al., 2007b), sperm motility (Aragon and Altamirano-Lozano, 2001), sperm counts (Aragon and Altamirano-Lozano, 2001; Chandra et al., 2007b; Llobet et al., 1993) and testosterone secretion (Chandra et al., 2007b, 2010), as well as increased percentage of abnormal spermatozoa (Aragon and Altamirano-Lozano, 2001; Chandra et al., 2007b). Also, vanadium compounds were found to induce DNA strand breaks both in vitro (Lloyd et al., 1998) and in vivo (Leopardi et al., 2005; Vijaya Bharathi et al., 2015).

In a Russian study, Skalnaya et al., reported a positive association between vanadium concentrations in semen and sperm count among 148 adult men (Skalnaya et al., 2015). Nevertheless, the results of this study may have been imprecise due to limited sample size. In an Austrian study, Ehrlich et al., assessed DNA strand breaks in the blood cells of 52 controls and workers from a vanadium pentoxide factory using the alkaline comet assay (Ehrlich et al., 2008). They found that tail moments and tail lengths in workers' leukocytes were significantly higher than in controls, suggesting that vanadium exposure causes DNA damage (Ehrlich et al., 2008). To date, however, no human investigations have assessed the associations between vanadium exposure at environmental levels and spermatozoa DNA integrity. The associations between vanadium exposure and serum reproductive hormones of adult men are also unclear.

Urinary excretion is the primary elimination route for vanadium from the human body (Chandra et al., 2007c); thus, urinary measures have been extensively used as exposure biomarkers (Health Canada, 2010; Fréry et al., 2011). Nevertheless, they may not directly represent the exposure levels of the male reproductive system. Vanadium has been reported to accumulate in the testes of rats after exposure and then reach a steady state (Fortoul et al., 2007; Mussali-Galante et al., 2005), indicating that concentrations of vanadium in seminal plasma may be reliable biomarkers of chronic vanadium exposure. Therefore, in this study, we simultaneously determined the concentrations of vanadium in seminal plasma and repeated urine samples and explored their associations with semen quality, spermatozoa DNA damage and serum reproductive hormones. In our previous studies among an overlapping population, urinary and seminal plasma cadmium and arsenic were associated with decreasing semen quality (Wang et al., 2016b, 2017b); urinary tin was associated with decreasing testosterone (T) (Wang et al., 2016c); and seminal plasma arsenic, selenium and copper were associated with spermatozoa DNA damage, whereas seminal plasma zinc was associated with increasing sperm concentration (Wang et al., 2017b). We thus also evaluated potential confounding by cadmium, arsenic, tin, selenium, copper and zinc on the associations between vanadium exposure and male reproductive health indicators.

2. Materials and methods

2.1. Study population

We recruited volunteers from male partners in subfertile couples who came to the Reproductive Centre of Tongji Hospital for semen examination (Wang et al., 2016b). Eligible men were between 18 and 55 years of age, had no self-reported diseases (e.g., epididymitis, orchiditis, vasectomy, varicocele, vesiculitis, undescended testicle, testis injury, adrenal disorder or diabetes) that may cause male reproductive disorders, and had no occupational exposure. We also excluded those who were azoospermia because its mechanism may be related to either a Y chromosome deletion or an obstruction. Between March and June 2013, 1052 men were enrolled. All men signed an informed consent form before participation. Of these volunteers, 746 men provided sufficient urine and seminal plasma for the simultaneous determination of vanadium concentrations, which were maintained in our current analysis. Each man finished a questionnaire at enrolment. The gathered data included socio-demographic factors (e.g., ethnicity, age, weight, height, educational level, household income), occupational exposure and medical history. This study was approved by the Human Studies Institutional Review Boards of Tongji Medical College.

2.2. Sample collection and laboratory measurements

Volunteers were required to give a semen specimen and two spot urine specimens and had a blood drawn at the reproductive centre on their clinic visit days. A single semen sample was gathered from all volunteers by masturbation into a trace-element-free polypropylene container. After liquefaction at 37 °C, aliquots were taken to determine the sperm quality parameters and perform neutral comet assay. Because of the high intra-day but relatively low inter-day variations in urinary concentrations of most metals/metalloids (Wang et al., 2016a, 2017a), repeated spot voids were collected into trace-element-free polypropylene cups from each man at different times within a given day (at least 2 h apart; mean duration of collections: 4.4 ± 3.7 h).

Semen were analysed for progressive sperm motility, total motility, concentration and sperm motion parameters (i.e., curvilinear velocity, straight-line velocity and linearity) using a micro-cell slide and computer-aided semen analysis according to the World Health Organization (WHO, 2010) guidelines as previously described (Wang et al., 2016b). Semen volume was determined using a trace-element-free polypropylene pipette. Total motility was the sum of progressive and non-progressive motility; the total count was calculated by multiplying sperm concentrations by the volumes. Sperm morphology was assessed on fixed and Papanicolaou stained smears under high-power magnification (1000×) with no fewer than 200 cells assessed per slide.