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Heavy metal contamination of prenatal vitamins

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ABSTRACT

Prenatal vitamins are often consumed daily during gestation and postnatally for up to 18–24 months with the belief that supplementation achieves better outcomes. Detrimental effects of gestational exposure to adverse chemical agents are gathering increasing attention. This study was designed to assess toxic element contamination in prenatal supplements.

Twenty-six commonly used prenatal vitamin brands including one prescription brand were collected from Canadian health-food outlets and pharmacies, and tested for toxic element contamination. Results were compared to established endpoints.

All samples contained Lead with average amounts being (0.535 µgm), 20/51 samples exceeded established standards for lead toxicity (0.50 µgm/day), with one sample yielding 4. µgm/day. Three samples registered inorganic arsenic levels above acceptable limits. Cadmium levels did not exceed current standards. Toxic elements such as Aluminum, Nickel, Titanium and Thallium were detected in all samples.

Cumulative intake of prenatal supplement over many months may constitute a significant source of toxic element exposure to the mother and offspring. With several samples exceeding known standards for gestational toxic element exposure, guidelines for routine monitoring and reporting are required. In keeping with recommendations from the International Federation of Obstetrics and Gynecology, industry regulation would be welcomed to protect expectant mothers and their vulnerable offspring.

1. Introduction and background

The gestational period on the continuum of human life is a phase of particular vulnerability to toxic exposures, including adverse chemical agents [1]. With the high toxicant-to-mass ratio of the fetus at a critical time of growth and development, adverse exposure during pregnancy presents a particular risk. Unfolding evidence in the medical literature confirms that toxicant exposures to reproductive-aged women and consequently to their developing progeny by vertical transmission are responsible for myriad developmental and long-term health problems [1–6].

Along with the recognition of potential fetal origins of chronic pediatric and adult disease [1–6], a constellation of three primary factors has contributed to the escalating concern regarding vertical transmission of toxic agents:

i) Epidemiological studies by major groups such as the Centers for Disease Control confirm that toxic chemical agents are now polluting the bodies to some degree of most men, women, children and newborns in North America [7,8];
ii) Recent research suggests that because of an immature detoxification capability, developing children in-utero may accrue and thus experience higher levels of toxicant exposure than their mothers [9].
iii) Most health professionals providing specialized maternity care do not explore myriad sources of gestational contamination as they lack training in environmental and toxicological determinants of fetal compromise [10].

Alongside concern about gestational exposures, there is increasing attention to natural health product (NHP) contamination, including toxicity within prenatal supplements [11]. It has become routine for most women in the developed world to consume a prenatal vitamin supplement to secure gestational nutrient sufficiency and to maximize pediatric health outcomes. Yet, it is known that a number of toxic metals and metalloids such as lead, cadmium, arsenic and mercury, sometimes found in NHPs, may result in adverse outcomes in pregnancy and the offspring [12–14].

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Recognizing the widespread threat and impact of toxic chemical exposures from myriad sources during pregnancy and lactation, the International Federation of Obstetrics and Gynecology (FIGO), an organization overseeing maternity health care throughout much of the world, has endeavored to focus concern to the issue of vertical transmission of toxic agents [15] and recommended that training on toxicants and environmental health become a fundamental part of health care education to diminish sources of adverse fetal exposure. This study was designed to research the possibility of toxic element contamination in a variety of commonly consumed prenatal supplements – a product ingested by most women in the developed world during gestation and lactation.

2. Methods

2.1. Collection of prenatal vitamins

Prenatal vitamins were collected from assorted retail outlets including several health food stores, pharmacies, as well as food retailers within a large metropolitan city – Edmonton, Alberta, Canada. All available prenatal brands found were acquired and included – no brands were excluded. Altogether, 26 varieties of prenatal vitamins were collected, with 16 samples having more than one lot number to determine intra-product variances. 51 samples in total were sent for analysis to ALS Scandinavia labs. Some products only had one lot number in multiple locations throughout the metropolitan area, and thus we were only able to test one batch of these particular brands.

2.2. Sample preparation for element analysis

For liquid products, samples were diluted 10-fold with 1.4 M HNO3 (SP grade). For solid products, approximately 0.25 g of sample were subjected to closed-vessel MW-assisted digestion (MARS-5 oven, 600W 1 h holding time) using 5 ml concentrated HNO3 (SP grade), 0.5 ml H2O2 (PA grade) and 0.02 ml HF (SP grade). After digestion, solutions were diluted with 1.4 M HNO3 (SP grade) providing a final dilution factor of approximately 500. A set of digestion blanks and matrix-matched CRM were prepared together with each digestion batch. All solutions were spiked with In (internal standard, at 2 µg/l) and analyzed by Inductively Coupled Plasma mass spectrometry using the state of the art Sector-Field High Resolution Mass Spectrometry ICP-SFMS (ELEMENT2, ThermoScientific) using combination of internal standardization and external calibration.

2.3. Sub–speciation for arsenic

0.7–1 g of a subsample was weighed into a 50 ml PE centrifuge tube and 10 ml of 0.1 M phosphoric acid in 50% methanol solution was added. The mixture was shaken overnight (> 16 h) on a mechanical shaking machine. The sample was then centrifuged at 3500 rpm for 5 min. The supernatant was filtered through with membrane (0.45 um pore size) into 12 ml polypropylene tubes. Aliquot of the extracts were then diluted 10 fold with MQ-water. Procedural blanks of 0.1 M phosphoric acid was also treated in the same way as samples. The final diluted solutions were transferred into HPLC vials.

Fresh mixed calibration standards of As(III) (arsenite), As(V) (arsenate), DMA (dimethylarsinate), and MMA (monomethylarsonate) at two concentration levels (at 5 and 10 ug/l) were prepared by serial dilutions from their respective individual 1000 mg/l stock solutions. To serve as a quality control, a mixed standard with concentration of 1 µg/l of each Quality Control Samples (QCS) and spiked samples were also prepared. MQ-water was used as calibration blank. The final calibration solutions QCS and spiked samples were transferred into High Performance Liquid Chromatography (HPLC) vials. For the HPLC separation of As species, a Hamilton PRP-X100 anion-exchange with gradient elution of 60 mM potassium phosphate was employed. Following the separation, post column eluent was mixed with stream of 1ug/l antimony (internal standard) in 10% nitric acid. The mixed solution then merges with a stream of 1% sodium borohydride in 0.2% sodium hydroxide solution to form volatile hydride. The gaseous hydride was purged by auxiliary argon to feed into the ICP-MS (Element 2 ICPMS system) for detection.

Integration of chromatographic peaks, construction of external calibration curve (linear regression) was carried out using the Xcalibur™ Software (Thermo Scientific).

3. Results

3.1. Minerals found in prenatal vitamins

Prenatal vitamins are generally a mixture of vitamins and minerals. Our analysis showed consistent findings of the listed minerals as outlined on the product label, although the amounts listed and the actual amounts in many samples varied considerably. This finding has previously been discussed with other research reported in the literature [16]. Further discussion on the minerals found in our prenatal samples tested and discussion of them in relation to the protection against assimilation of toxic minerals [17] will be reserved for subsequent publications.

3.2. Toxic elements found in prenatal vitamins

There are established upper limits of ingestion on a daily basis of toxic elements from various organizations. However, few organizations have set limits for reproductive toxicity in relation to gestational and/or lactational exposure. The most stringent are from Proposition 65 in California and the US Pharmacopeia as listed in Table 1.

This discussion will be limited to the more common toxic metals and metalloids including mercury (Hg), lead (Pb), arsenic (As), cadmium (Cd), and aluminum (Al), as well as some emerging toxic elements such as Nickel (Ni), Titanium (Ti) and Thallium (Tl) as outlined in Table 2.

3.2.1. Mercury

Mercury was detected in 14/50 samples but levels were well within acceptable standards (< 0.3 µgm/day) with the highest level of exposure at 0.095 µgm/day. Levels below 0.3 µgm/day are considered to be within acceptable limits.

3.2.2. Lead

All 51 samples provided more than 0.1 µgm/day of Pb exposure. The overall average amount was 0.535 µgm/day, above the Proposition 65 limit (P65L) of 0.5 µgm/day for prenatal vitamins. Of the 26 products analyzed, 14 (more than half of the samples tested) had higher levels, with one product providing 4.0 µgm/day. Cumulative exposure per pregnancy (including 90 days preconception and 270 lactational days) was about 341 µgm on average, and 2.56 mg for the brand with the highest amount of Pb.

3.2.3. Cadmium

All of the 51 samples had some level of Cd. The average in all products was 0.37 µgm/day. Eight of the 26 products resulted in exposure levels greater than 0.5 µgm/day; these levels, however, were all below the P65 and USP accepted levels.

3.2.4. Arsenic

All 51 samples had some level of total As with an average exposure of 0.42 µgm/day. Four samples had more than 1.0 µgm/day exposure. On As speciation sub-analysis of these four samples, however, most of this arsenic was organic (considered much less toxic) rather than the highly toxic inorganic form. When considering the inorganic As species, of the 4 samples tested, nonetheless, 3/4 samples had > 0.1 µgm/day–above the acceptable (P65L) limit, with one having 0.4 µgm/day of