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Short communication

A pilot study of seafood consumption and exposure to mercury, lead, cadmium and arsenic among infertile couples undergoing *in vitro* fertilization (IVF)

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ABSTRACT

This cross-sectional pilot study was conducted to assess environmental exposures to toxic elements through seafood consumption, among infertile couples undergoing *in vitro* fertilization (IVF). Twenty-five women and 15 men completed a questionnaire, and provided biologic specimens for quantification of Hg, Pb, Cd, and As using ICP-MS. Consumption of 'mollusks' and 'shellfish' are associated with increased blood Hg. Other seafood consumption predicts blood Pb, and urine Cd and As. Though limited by small numbers and the cross-sectional design, these results suggest that consumption of specific seafood items increases exposure to toxic elements in couples undergoing IVF.

1. Introduction

Evidence suggests that couples undergoing infertility treatment are at increased risk for adverse reproductive effects (Younglai et al., 2005), from the widely distributed toxic elements (CDC, 2012) mercury (Hg), lead (Pb), cadmium (Cd) and arsenic (As). Dietary intake, especially seafood, is an important source of exposure to toxic elements for much of the U.S. (MacIntosh et al., 1996). To our knowledge, no previous study has characterized specific sources of exposure in a U.S. IVF population. In this pilot study, we measured concentrations of total Hg, Pb, Cd, and total As in the blood or urine of infertile couples undergoing *in vitro* fertilization (IVF), as biomarkers to assess exposure from the consumption of specific seafood items and other sources.

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2. Materials and methods

2.1. Sample selection

Study participants comprise a subsample of the previously described Study of Metals and Assisted Reproductive Technologies (SMART) (Bloom et al., 2010). Briefly, 58 women and 36 men completing a first IVF cycle at the University of California at San Francisco (UCSF) Center for Reproductive Health between March 12th, 2007 and April 27th, 2008 were recruited. Twenty-five female patients and 15 male partners who completed a study questionnaire on the day of oocyte retrieval, and who also provided blood and urine for the determination of trace elements were included in this study. The study protocol was approved by the UCSF Committee for Human Research.

2.2. Study questionnaire and exposure variables

The study questionnaire assessed consumption of specific seafood items and health behaviors likely to lead to exposure. Demographics and the frequency of consumption for 51 seafood items during the week of study participation were queried, as were non-seafood exposures. Given small numbers, reported seafood consumption was collapsed into 14 non-exclusive categories, using three approaches: (1) 'any' type of seafood as described by Fig. 1a; (2) seven preparation categories as described by Fig. 1b; and (3) six seafood 'type' categories as described by Fig. 1c. Seven additional non-seafood exposure variables were created, including 'cigarette smoking,' 'other (non-dietary) exposure to Hg,' presence of 'Hg dental amalgams,' use of Hg-based 'skin-lightening creams,' use of 'Chinese medicine' preparations, use of 'fish supplements,' and greater 'summertime fish' consumption.

2.3. Laboratory analysis

Collection and analysis of biological specimens was previously described in detail (Bloom et al., 2010; Kim et al., 2011). Briefly, fasting whole blood and 'spot' urine specimens were collected from women at the time of oocyte retrieval, and in non-fasting fashion from men on the same day. Blood and urine specimens were analyzed for total Hg and Pb using a Perkin Elmer Sciex ELAN DRC II inductively coupled plasma-mass spectrometer (DRC-ICP-MS) (PerkinElmer Life and Analytical Sciences, Shelton, CT, USA) with Dynamic Reaction Cell technology.

2.4. Statistical analysis

Multiple linear regression models were used to identify exposure variables predictive of elements as dependent variables, with consideration of important covariates. A log-transformation, with the addition of a constant was applied as appropriate. For each element three strategies were used: (1) the 'any' seafood variable was forced into the model and a stepwise model selection procedure used to incorporate non-seafood variables as potential predictors; (2) a stepwise model selection procedure was used to identify predictors from the seafood 'preparation' categories as well as the non-seafood variables; and (3) a stepwise model selection procedure was used to identify predictors from the seafood 'type' categories as well as the non-seafood variables. Predictors entered models during the forward stepwise process at $p < 0.05$ and were retained if $p < 0.10$. Should no predictor have been retained, these entry/exit criteria were relaxed by increments of 0.05 up to $p < 0.15/0.20$. Known predictors of element levels were forced as covariates into all regression models prior to stepwise selection, including sex and race for all elements (Kim et al., 2011), age for Hg, Pb and Cd, smoking for Cd, and creatinine for urine elements (Boeniger et al., 1993). SAS v.9.2 (SAS Institute Inc., Cary, NC, USA) was used for statistical analysis with significance defined as $p < 0.10$.

3. Results

The median age is 34 years (range 28–44) for women and 37 years (range 31–48) for men. Approximately 17% ($n = 4$) of women and 13% ($n = 2$) of men are either current or former cigarette smokers. A lower proportion of men (13%, $n = 2$) are Asian than are women (24%, $n = 6$). Blood Pb is lower among women ($p = 0.08$), and increases with age ($r = 0.41$, $p = 0.07$). Urine Cd levels are higher among women ($p < 0.0001$), and among smokers (median = 0.08 μg/g creatinine, $p = 0.51$), yet not of significance. Most elements exceed the limits of detection (>73%); blood Hg and urine As are inter-correlated ($r = 0.57$, $p = 0.002$). Many participants (≥84.0%) report consumption of at least one seafood item, whereas half report exposure to at least one non-seafood source of Hg.

Table 1 describes multivariable linear regression models for Hg, Pb, Cd, and As. Consumption of 'any' seafood item is a positive predictor for Hg (blood Hg model 1). Consumption of 'shellfish' is retained as a significant positive predictor in the 'preparation' model (blood Hg model 2), and 'tuna' and 'mollusks' are retained as positive predictors in the 'type' model (blood Hg model 3). Consumption of 'any' seafood item is not associated with Pb (blood Pb model 1). Yet, consumption of 'steak' increases and 'farmed' seafood items decreases Pb in the 'preparation' model (blood Pb model 2). Nor is there any association between the consumption of 'any' seafood and Cd (urine Cd model 1). However, 'sashimi' consumption in the 'preparation' model (urine Cd model 2) and 'tuna' consumption in the 'type' model (urine Cd model 3) are negative predictors. In all Cd models, weak positive associations are detected for use of 'fish supplements.' 'Any' seafood is unrelated to levels of As (urine As model 1), but As is increased among 'canned' seafood items consumers, and decreased among 'raw' seafood consumers in the 'preparation' model (urine As model 2).

4. Discussion

Seafood is an important and well-recognized source of dietary Hg exposure (Mahaffey et al., 2009). Our multivariable linear regression modeling for blood Hg indicates that consumption of 'any' seafood item, 'shellfish,' and 'mollusks' are associated with higher blood Hg, though these categories are not mutually exclusive. Elevated MeHg concentrations in predatory fish species are widely reported in the U.S., yet exposure