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Essential and toxic element concentrations in blood and urine and their associations with diet: Results from a Norwegian population study including high-consumers of seafood and game

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HIGHLIGHTS

- A study on interplay and sources of six different elements
- The elements are selenium, iodine, arsenic, mercury, cadmium and lead.
- Exposures did not give rise to nutritional or toxicological concerns.
- A distinct pattern of associated biological markers was found including four elements.
- The pattern, including iodine, selenium, arsenic and mercury reflected seafood intake.

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ABSTRACT

The first aim of the study was to evaluate calculated dietary intake and concentrations measured in blood or urine of essential and toxic elements in relation to nutritional and toxicological reference values. The second aim was to identify patterns of the element concentrations in blood and urine and to identify possible dietary determinants of the concentrations of these elements. Adults with a known high consumption of environmental contaminants (n = 111), and a random sample of controls (n = 76) answered a validated food frequency questionnaire (FFQ). Complete data on biological measures were available for 179 individuals. Blood and urine samples were analyzed for selenium, iodine, arsenic, mercury, cadmium and lead. Principal component analysis was used to identify underlying patterns of correlated blood and urine concentrations. The calculated intakes of selenium, iodine, inorganic arsenic and mercury were within guideline levels. For cadmium 24% of the high consumer group and 8% of the control group had intakes above the tolerable weekly intake. Concentrations of lead in blood exceeded the bench-mark dose lower confidence limits for some participants. However, overall, the examined exposures did not give rise to nutritional or toxicological concerns. Game consumption was associated with lead in blood (B_{ln} 0.021; 95%CI:0.010, 0.031) and wine consumption. Seafood consumption was associated with urinary cadmium in non-smokers (B_{ln} 0.009; 95%CI:0.003, 0.015). A novel finding was a distinct pattern of positively associated biological markers, comprising iodine, selenium, arsenic and mercury (eigenvalue 3.8), reflecting seafood intake (B 0.007; 95%CI:0.004, 0.010). The study clearly demonstrates the significance of seafood as a source of both essential nutrients and toxic elements simultaneously and shows that exposure to various essential and toxic elements can be intertwined.

Abbreviations: As, arsenic; BMD, benchmark dose; BMDL, benchmark dose (lower confidence limit); BMI, body mass index; Cd, cadmium; EFSA, European Food Safety Authority; FFQ, food frequency questionnaire; Hg, mercury; I, iodine; JECFA, Joint FAO/WHO Expert Committee on Food Additives; NFG Study, Norwegian Fish and Game Study; NIFES, National Institute of Nutrition and Seafood Research; NNR, Nordic Nutrition Recommendations; Pb, lead; PCB, polychlorinated biphenyl; PoP, persistent organic pollutants; PTWI, provisional tolerable weekly intake; S-Fe, serum ferritin; Se, selenium; TWI, tolerable weekly intake.

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1. Introduction

Humans are exposed to chemical elements, both essential and toxic, from food, air and water. In non-occupationally exposed individuals, food is undoubtedly the most important source of many of the essential and toxic elements (Cornelis et al., 1996). Tolerable intake levels have been set for many toxic compounds in food, while recommended daily intakes have been set for the nutrients. Blood and urinary concentrations may serve as biomarkers of on-going exposure or body burden (EFSA, 2011, 2012, 2009a, 2009b, 2010; NNR, 2004). Urinary excretion best reflect exposure to iodine (I), arsenic (As) and *inorganic* mercury (iHg), whereas for selenium (Se), *methyl* mercury (MeHg) and lead (Pb), blood concentrations better reflect exposure. Cadmium (Cd) in urine is mainly a biomarker of body burden, whilst Cd in blood better reflects on-going exposure (Cornelis et al., 1996; IOM, 2000, 2001). There is increasing evidence that nutritional factors can modulate the kinetics and toxicity of undesirable elements such as As, mercury (Hg), Cd and Pb and thus impact health and disease outcomes associated with exposure to these elements (Cory-Slechta, 2005; Furst, 2002; Meltzer et al., 2010; Peraza et al., 1998). Studies investigating several elements simultaneously might provide important information about interactions between dietary factors which are not detected when working with one element at a time.

The Norwegian Fish and Game Study (NFG Study) was designed to investigate the exposure to food-derived environmental contaminants in 27 municipalities in which fishing and hunting are common, with the aim to study a wide range of intakes. In a follow up study of a subgroup within NFG Study, participants donated blood and urine samples which were analyzed for both environmental contaminants and nutrients. The participants also filled in a validated food frequency questionnaire (FFQ) and answered questions on socio-demographic factors (Brantsæter et al., 2008; Kvalem et al., 2009). This gave an opportunity to investigate patterns of elements known to be associated with consumption of fish and/or game i.e. Se, I, As, Hg, Cd and Pb (Brantsæter et al., 2010; Miklavcic et al., 2013; Taggart et al., 2011), and their association with socio-demographic factors and diet. Previous papers from the NGF Study have mainly focused on persistent organic pollutants (PoPs) (Birgisdottir et al., 2012; Haug et al., 2010; Knutsen et al., 2008; Kvalem et al., 2009) as well as a study on determinants of Hg in blood (Jenssen et al., 2012). The first aim of the current study was to assess if the intake or concentrations in blood or urine of the essential and toxic elements in focus would give rise to concern from a nutritional or toxicological standpoint. The second aim was to identify patterns of their concentrations in blood and urine and to study if the patterns were associated with dietary determinants, with focus on fish and game consumption.

2. Materials and methods

2.1. The Norwegian Fish and Game Study

The NFG Study was initiated to evaluate the dietary distribution of environmental contaminants in the Norwegian population. The study was performed in three parts, where part A included a random sample of the whole population, and part B included participants from 27 coastal and inland municipalities in Norway with ample supplies of fish and/or game but without known point source of persistent organic pollutants and toxic elements (Bergsten C, 2005). Participants in part B with high consumption of food items known to contain relatively high concentration of dioxins, polychlorinated biphenyls (PCBs), Hg or Cd were invited to participate in part C (n = 434). Additionally, a random sample of participants from part B was invited to part C as a reference group (n = 267). This selection of participants was done to secure both enough participants with a presumed high intake of the contaminants as well as a wide range of dietary exposure. The study design is novel and further details about results from part C of the study have been published previously (Knutsen et al., 2008; Kvalem et al., 2009). The response rate was close to 28% for both groups, resulting in 117 participants in the group with an expected high intake of contaminants and 77 participants in the reference group. A comparison of those who accepted the invitation to participate and those who did not revealed that the participants were slightly older (50 vs. 46 years), and included a higher percentage of university graduates (36% vs. 28%), than the non-participants.

2.2. Implementation

The study was conducted in 2003. Participants were contacted by mail and gave written informed consent in accordance with the Helsinki Declaration. The participants answered a 12 page semi-quantitative food frequency questionnaire (FFQ) and a one-page demographic questionnaire. Each participant made an appointment with their own physician to obtain a blood sample in vacutainers provided by the researchers. A morning spot urine sample was obtained the same day and delivered to the physician who mailed the biological samples to the study centre. The study protocol was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate (id: S-02138).

2.3. Food frequency questionnaire

The FFQ was adapted to Norwegian food traditions and covered the habitual diet during the last twelve months (Meltzer et al., 2008). The questionnaire has been thoroughly validated in a subgroup of pregnant women in the Norwegian Mother and Child Cohort Study (MoBa), and was found to be a valid tool for ranking participants according to high and low intakes of foods, energy and nutrients (Brantsæter et al., 2008). The FFQ contained questions about 233 food items or meals, including highly detailed questions on seafood and game. Questions about the use of dietary supplements were also included. Food and beverage consumption (g/day) were aggregated into 41 non-overlapping food groups, based on structure, nutrient profile or culinary usage. Of these, nine pertained to seafood; lean fish, semi-oily fish, oily fish, fish liver, fish liver *pâté*, roe, shrimp, crustacean and crab. Food groups pertaining to consumption of game were: grouse, reindeer, moose and deer, and organ meat from game. The questionnaires were optically read, food frequencies were converted to food amounts and FoodCalc (Lauritsen, 2006) was used for estimating intakes of nutrients and contaminants. Four participants were excluded from analysis due to unlikely energy intakes (less than 4.5 MJ/day or more than 20 MJ/day).

2.4. Databases

The Norwegian food composition table (Norwegian Food Safety Authority et al., 2003) was used to calculate energy and Se intakes. At the time of the study the food composition table was not complete and the concentration of I in a number of foods was added to the database at the Norwegian Public Health Institute (Brantsæter et al., 2010). Additionally, a database of dietary supplements was developed for the calculation of nutrients from supplements (Brantsæter et al., 2007). Moreover, databases for *total* Hg, *total* As and Cd were compiled especially for the NFG Study. The database on the *total* As content in food included data from Norwegian measurements of seafood between 2000 and 2003 i.e., around the time of the study. However, if data was missing for a seafood item, measurements up to year 2006 were used (NIFES, 2011). For other food groups, data on *total* As was mainly obtained from analyses performed in Canada, as such data was not available in Norway (Dabeka et al., 1993; Uneyama et al., 2007). The collection of the database for concentration of Hg in Norwegian food has been described previously