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Mercury, arsenic and selenium exposure levels in relation to fish consumption in the Mediterranean area

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ABSTRACT

In order to assess mercury (Hg), selenium (Se) and arsenic (As) exposure in the Mediterranean area, total mercury (THg), monomethylmercury (MeHg), Se and As levels were measured in umbilical cord blood and breast milk from Italian (n=900), Slovenian (n=584), Croatian (n=234) and Greek (n=484) women. THg, MeHg, As, and Se levels were also determined in blood samples of the same mothers from Italy and Croatia. In addition, THg and MeHg were determined in the same women's hair from all the countries involved in this study and As and Se levels were determined in the mother's urine samples from Italy, Croatia and Greece. Besides recording the consumption of other food items, the frequencies of fish consumption were assessed by detailed food frequency questionnaires, since fish represents an important source of Hg, Se and As in humans. The highest levels of THg and As were found in cord blood ($Med_{(THg)}$=5.8 ng/g; $Med_{(As)}$=3.3 ng/g) and breast milk ($Med_{(THg)}$=0.6 ng/g; $Med_{(As)}$=0.8 ng/g) from Greek women, while the highest Se levels were found in cord blood (Med=113 ng/g) from Italy. Significant linear correlations were found between Hg, Se and As in blood, cord blood and breast milk. In addition, significant relations were found between the frequencies of total fish consumption and biomarkers of As, MeHg and Se exposure, with the strongest Spearman rank coefficients between frequencies of total fish consumption and THg levels in cord blood (r_s=0.442, $p<0.001$) or THg levels in hair (r_s=0.421, $p<0.001$), and between frequencies of total fish consumption and As levels in cord blood (r_s=0.350, $p<0.001$). The differences in Hg and As exposure between countries were probably due to different amounts of fish consumption and the consumption of different species of fish of different origin, while the highest Se levels in women from Italy were probably the consequence of the more frequent consumption of different non specific food items. Moreover, fish consumption, the possible common source of As, Hg and Se intake, could explain the correlations between the elements determined in cord blood, mother's blood or breast milk.

1. Introduction

An important source of Hg, Se and As exposure in man is the consumption of fish and other food sea (UNEP, 2002; Hughes et al., 2009; Reilly, 1996).

Although inorganic Hg it is also present in fish (Miklavčič et al., 2011a), MeHg is of particular concern because it can build up in fish higher in the food chain and marine mammals to levels that are many times higher than the levels in the surrounding water, also to levels exceeding what is regarded as safe (Horvat et al., 2011a). Moreover, 95% of MeHg is to be absorbed in the gastrointestinal tract, while animal studies indicate that the absorption of inorganic Hg is approximately 10–30% (Piotrowski et al., 1992; Morcillo and Santamaria, 1995). Overall, the general population is

Abbreviations: CRM, certified reference material; k, coverage factor; LOD, limit of detection; LOQ, limit of quantification; Max, maximum; Min, minimum; Med, median; MeHg, monomethylmercury; P5, 5th percentile; P95, 95th percentile; PHIME, Public Health Impact of Long-term Low-level Mixed Element Exposure in Susceptible Population Strata; PUFAs, polyunsaturated fatty acids; RM, reference material; THg, total mercury; X, mean

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exposed to MeHg mainly through the consumption of freshwater and marine fish, and consumption of other animals that consume fish (EPA, 1997a,b, 2003; UNEP, 2002). The levels of Hg in fish from different FAO regions ranged from 0.003 to 1.110 mg/kg (Miklavčič et al., 2011a). The highest levels are found in fish of older age that are apical predators, such as king mackerel, pike, shark, swordfish, walleye, barracuda, large tuna, scabbard, marlin and fish-consuming mammals such as seals and toothed whales (EPA, 1997a,b, 2003; UNEP, 2002; Miklavčič et al., 2011a). Commonly used cooking techniques including panfrying, deep-frying, baking, boiling, and smoking do not appreciably reduce the Hg content of the fillet portion of fish (Morgan et al., 1997; Perelló et al., 2008). The major toxic effect of MeHg is on the central nervous system and the developing foetus is the most vulnerable target (NRC, 2000). Scalp hair has been widely used as a good indicator of MeHg exposure. Hg in umbilical cord blood is preferentially measured instead of Hg in maternal blood for prenatal MeHg exposure assessment (Horvat et al., 2011a).

For most people, excluding sources of As pollution and drinking water contamination, the diet is the major source of As (Abernathy et al., 2003). The levels of As vary widely in different foods and are dependent on the type of soil, water and geochemical activity (ASTDR, 2007). Foods of marine origin, such as fish and shellfish, tend to have the highest levels of As, primarily in organic form such as arsenobetaine and arsenocholine (Hughes et al., 2009). Tuna, shrimp, hake and sardine have levels of As ranging from 0.3 to 2.7 mg/kg (Tao and Bolger, 1999; Perelló et al., 2008). Compared to inorganic As, the organic forms of As in seafood are considered relatively nontoxic (Sakurai et al., 1997; Hughes et al., 2009). The prevalent species of As that occurs in marine organisms, arsenobetaine (Edmonds and Francesconi, 2003) is rapidly excreted by humans unchanged (Vahter, 1994) and is assumed to have negligible toxicity because of its high LD50 in mice ($>10\ 000$ mg/kg) (Kaise and Fukuit, 1992). In contrast to organic As, it was demonstrated that inorganic As is associated with increased risk for a wide range of diseases. To date, it has been linked to high risks of several types of cancer, as well as of diabetes, vascular disease, hypertension, neurological disorders, reproductive problems, and the well-known skin damage (Hopenhayn, 2006; NRC, 1999; IARC, 2000). Inorganic As is predominant in drinking water (Hopenhayn, 2006) or to a lesser extent in foods such as rice, flour, grape juice and spinach (Schoof et al., 1999). Different studies reported decreases or increases in total As after cooking (Devesa et al., 2001; Van Eltern and Šlejkovec, 1997; Perelló et al., 2008). The increase in As levels could be only apparent due to loss of water, while solubilisation or volatilization of As compounds during cooking may cause a decrease in the concentration of As (Devesa et al., 2001). Biomarkers of As exposure include the concentration in urine, blood, hair, or nails. The most common inorganic As biomarker of exposure is total As in urine. However, consumption of seafood containing high levels of organic As can critically confound estimation of inorganic As exposure. Analysis of blood for As is best suited for recent high-dose exposure and cannot be a reliable biomarker for inorganic As exposure because it is cleared so rapidly, particularly at low levels of inorganic As exposure (ASTDR, 2007; Hughes, 2002; Horvat et al., 2011b).

Se is an essential trace element, but be toxic in larger amounts. The range between insufficiency and toxicity is rather narrow. A Joint Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert Committee on Human Vitamin and Mineral Requirements proposed a recommended nutrient intake for Se of 26 and 34 μg/day in adult women (55 kg) and men (65 kg), respectively, and 6 μg/day in infants aged 0–6 months (6 kg) (Joint FAO/WHO, 1998). However, different intuitions recommended different values. The recommended adequate intakes of selenium published by D_A_CH are 30–70 μg/day for adults, 4–15 μg/day until infants are 6 months old and 7–30 μg/day for infants aged 4 to 12 months (Reference Values for Nutrition Intake, 2002). Fish and other seafood are the most important providers of Se in the human diet (Reilly, 1996) and the levels vary greatly according to species and fishing area (Wyatt et al., 1996). Total Se levels found in fish from different FAO regions ranged from 0.085 mg/kg to 1.180 mg/kg (Miklavčič et al., 2011a). Beside fish, food items high in Se can include meat, nuts, cereals and bread. Importantly, the Se content of foods can be extremely variable, depending on the combination of geo-environmental factors and Se supplementation of fertilizers and animal feedstuffs (Barclay et al., 1995; Thomson and Robertson, 1990; NIH, 2011; Smrkolj et al., 2005). Foods normally contain only organoselenium compounds. Inorganic compounds of the element, such as sodium selenite, only enter the diet as supplements or contaminants (Reilly, 1996). Plasma, erythrocyte and whole-blood Se respond to changes in Se intake. More large, high quality, randomized controlled trials are needed for Se biomarkers to explore heterogeneity in response to Se intakes (Ashton et al., 2009). Several studies have shown Se supplementation counteracts the negative impacts of exposure to Hg in all investigated species of mammals, birds and fish (Beijer and Jernelov, 1987; Culvin-Aralar and Furness, 1991). However, little is known about the potential protective effects of dietary Se against MeHg neurotoxicity in humans (NRC, 2000). Antagonistic effects or mutual detoxification between As and Se have also been confirmed in many animal species including humans (Levander, 1977; Zeng., 2001; Zeng et al., 2005). The interaction between Se and As can occur directly and indirectly, depending on the chemical forms and dose of each. Increased biliary excretion of Se may be the principal mechanism by which As interacts with Se. The existence of an interaction between As and Se through biliary excretion at low level Se and As intakes still remains to be determined (Zeng et al., 2005).

Although fish are a source of pollutants such as toxic metals (Hg, As, lead and cadmium), polychlorinated biphenyls, organochlorine pesticides and aromatic hydrocarbons, they are also an important source of protein, microelements (Se, iodine, zinc), macroelements (calcium, phosphorus), polyunsaturated fatty acids (PUFAs) and fat-soluble vitamins. While Hg in fish negatively affects neurodevelopment (NRC, 2000), PUFAs in fish have a potential beneficial effect on neurological development (Nettleton, 1993; Helland et al., 2008). A considerable body of literature exists focused on the effects of prenatal exposure through fish consumption on neurodevelopment. However, the findings are inconsistent, particularly when assessing effects at low levels of exposure (Schoeman et al., 2009). Some of the divergent outcomes from different studies could be due to different end points and ages used in testing, use of different biomarkers, choice of covariates for statistical models, differences in the study populations and different levels of Hg and other contaminants in fish (Schoeman et al., 2009).

The objective of this study was to assess the Hg, As and Se exposure of the most susceptible population of Mediterranean areas, namely pregnant women, through fish consumption using detailed fish consumption data in combination with different biomarkers of exposure. The main strength of this study is the high number of women (over 2000) from whom different biomarkers of Hg, As and Se exposure and nutritional status data were collected. Although a small part of the data on Hg exposure in Slovenia has already been published elsewhere (Miklavčič et al., 2011b); this is a comprehensive study that involves the same data collection approach and the same sampling methods in all the four countries and in which analysis of all biological samples was performed by the same laboratory. Furthermore, in terms of simultaneous low-level exposure to a group of elements that can interact with each other, this study represents invaluable