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Nutrition

Umbilical cord blood and placental mercury, selenium and selenoprotein expression in relation to maternal fish consumption

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ABSTRACT

Seafood is an important source of nutrients for fetal neurodevelopment. Most individuals are exposed to the toxic element mercury through seafood. Due to the neurotoxic effects of mercury, United States government agencies recommend no more than 340 g (12 oz) per week of seafood consumption during pregnancy. However, recent studies have shown that selenium, also abundant in seafood, can have protective effects against mercury toxicity. In this study, we analyzed mercury and selenium levels and selenoprotein mRNA, protein, and activity in placenta of a cohort of women in Hawaii in relation to maternal seafood consumption assessed with dietary surveys. Fish consumption resulted in differences in mercury levels in placenta and cord blood. When taken as a group, those who consumed no fish exhibited the lowest mercury levels in placenta and cord blood. However, there were numerous individuals who either had higher mercury with no fish consumption or lower mercury with high fish consumption, indicating a lack of correlation. Placental expression of selenoprotein mRNAs, proteins and enzyme activity was not statistically different in any region among the different dietary groups. While the absence of seafood consumption correlates with lower average placental and cord blood mercury levels, no strong correlations were seen between seafood consumption or its absence and the levels of either selenoproteins or selenoenzyme activity.

Introduction

High mercury (Hg) exposures are well known for their toxic effects on human health as seen in events of contamination in Minamata, Japan and in Iraq [1–4]. Exposures to such high amounts of Hg are now extremely uncommon, but the potential effects of low-level MeHg exposures remain controversial. The largest contributor to Hg in the atmosphere is coal-burning power plants [5]. After Hg is released into the air and settles into sources of water, microorganisms convert it to MeHg, which accumulates in small fish and bioaccumulates in predatory species with the highest levels being observed in sharks and toothed whales. For most individuals, primary exposure to MeHg is through seafood [6]. Epidemiological studies in the Faroe Islands and New Zealand report adverse effects associated with increasing maternal seafood MeHg exposures [7,8] whereas studies in the Seychelle Islands and Bristol, United Kingdom report seafood consumption is associated with beneficial, rather than adverse outcomes in prenatally exposed children [9,10].

Studies of catastrophically high MeHg exposures in Japan [11,12] and Iraq [3,4] and unusually high MeHg exposures from shark meats eaten in New Zealand [13] or pilot whale meats eaten in the Faroe Islands [14,15] demonstrated that maternal MeHg exposure during pregnancy correspond with neurodevelopmental outcome defects (amounting to ~0.1 IQ points) subsequently observed in the children of exposed mothers. However, studies of ocean fish consumption in the Seychelles [16–18] found beneficial effects on child development associated with higher levels of maternal fish consumption and greater amounts of MeHg than those observed in the Faroe Islands study [19]. The largest, most comprehensive study of this issue found increasing maternal seafood consumption in the United Kingdom was associated with substantial beneficial effects [20] that increased child IQ's by as

Abbreviations: Dio, iodothyronine deiodinase; EPA, Environmental Protection Agency; GPx, glutathione peroxidase; Hg, mercury; MeHg, methylmercury; NRC, National Research Council; Se, selenium; Sel, selenoprotein; TrxR, thioredoxin reductase; UBC, ubiquitin C.

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much as 5 points [9]. A smaller study conducted in the United States found IQ's of children whose mothers consumed the most seafood during pregnancy were similarly increased [21]. These effects are not attributed to MeHg exposure, but are instead thought to occur as a result of improved maternal nutritional intakes.

Based largely on the Faroe Islands study, the Federal Drug Administration (FDA) and National Research Council (NRC) in the United States issued seafood consumption advice in 2004 recommending that women who might become pregnant, pregnant women, nursing mothers, and young children should consume no more than 12 oz of low Hg seafood per week and to avoid eating shark, swordfish, king mackerel, or tilefish because of their high MeHg levels [22]. Although meant to protect children of fish consuming populations, mothers that take this advice to the extreme of avoiding seafood altogether could actually harm their own health and diminish child neurodevelopmental outcomes [9,10,23]. Seafood is an important source of polyunsaturated fatty acids, which are essential for the neurodevelopment of a growing fetus [8,9,24]. Additional risks that have been linked to decreased fish consumption and corresponding low omega-3 fatty acid levels are preeclampsia and premature delivery [9,25].

Seafood is also an important source of other nutrients including vitamin D and selenium (Se). Selenium is incorporated into the amino acid selenocysteine, which is required in the active sites of enzymes that prevent and/or reverse oxidative damage in brain tissues of all forms of animal life with recognizable nervous systems. These enzymes include the glutathione peroxidases (GPx), thioredoxin reductases (TRx), and methionine R sulfoxide reductase. Dietary Se deficiency or decreased Se bioavailability result in decreases in selenoprotein levels and selenoenzyme activities. Reduced Se levels and placental glutathione peroxidase activity have been observed in preeclamptic versus normotensive placenta [26]. In addition, it is well documented that the mRNA levels for several selenoproteins are regulated by dietary Se [27,28]. Thus, analysis of selenoprotein mRNAs, proteins, and enzymatic activities provides three independent assessments of dietary Se status and Se bioavailability.

Recent studies signify supplemental Se's ability to mitigate Hg toxicity [29], and high MeHg exposures can irreversibly inhibit critical Se-dependent enzymes, leaving vulnerable tissues of the brain and neuroendocrine organs inadequately protected against oxidative damage [30]. Therefore, MeHg-dependent inhibition of Se-dependent enzymes is a major contributing cause, and may be the exclusive cause of the adverse child outcomes that occur in mothers that eat pilot whale or shark meats with disproportionately high Hg:Se molar ratios. Supplemental Se is able to replace the Se bound by MeHg, ameliorating or preventing MeHg toxicity in all species of animals, birds, fish and invertebrates that have been tested [29,31]. Selenium is naturally present in all foods, but is especially abundant in ocean fish, and greatly exceeds MeHg levels in all but a few predatory species, e.g., mako shark [25].

The current pilot study was conducted to investigate the correlations between maternal fish consumption, Hg, Se, and omega-3 fatty acids in cord blood and placentas from a cohort of women in Hawaii [32]. This report is a secondary analysis, with the objective of investigating the correlations between the dietary recall of seafood consumption and placental Se status and antioxidant selenoenzyme protein and activity levels. Our results show that while the absence of seafood consumption correlates with lower placental and cord blood Hg levels, no correlations were seen between seafood consumption or its absence and the levels of either selenoproteins or selenoenzyme activity. This information, along with the known benefits of fish consumption from previous studies, provides crucial insights that should help to dispel the misinformation about the potential risks of seafood consumption during pregnancy.

Materials and methods

Subjects and enrollment

All women who presented to the Kapiolani Medical Center Labor and Delivery suite between June 2010 and March 2011 were assessed for eligibility to participate. Participants were considered eligible if they met the following criteria: age 18–45 years old, in labor with a live singleton fetus, gestational age ≥37 weeks, and not a cord blood donor. In addition, because specimens had to be processed within 2 h of delivery, only women who ultimately delivered when laboratory assistants were available were eligible for participation. Women who reported tobacco, alcohol, or illicit drug use or chronic medical conditions were excluded. Patients who met eligibility criteria were approached about participating in the study. The first 100 to consent to participation were included. Patients were concomitantly enrolled in the Hawaii Biospecimen Repository, and all demographic and clinical data obtained via the repository project were available for this study. Either intrapartum or after delivery, patients were asked to complete a dietary survey of their fish and seafood consumption during their pregnancy. Women were asked to quantify the amount of seafood they had eaten by recording how many times they had eaten seafood in the last month and approximately how much they typically ate in each instance (they were informed that 3 oz is approximately the size of a deck of cards). Total fish consumption in the last month was calculated by multiplying the number of times the women reported eating seafood by the amount of seafood they typically ate during each meal.

Sample collection

After delivery, a single tube of approximately 14 mL of whole blood was collected from the umbilical cord in a standard EDTA tube. Samples were processed within 2 h of delivery and 2 mL was aliquoted and stored at −25 °C for Hg and Se assays. The rest of the sample was centrifuged and the red cell fraction was separated into aliquots that were stored at −80 °C for omega-3 fatty acid analyses. Samples of placental tissue were obtained from regions proximal and peripheral to the umbilical cord, and frozen in liquid nitrogen within 2 h of delivery, then transferred to freezers for storage at −80 °C.

Mercury and selenium sample analysis

Umbilical cord blood and placental tissue samples collected were shipped to the Energy & Environmental Research Center at the University of North Dakota. Individual samples of blood and placental tissue (~0.25 g) were weighed into single-use, trace element-free 50-mL digestion tubes (Environmental Express, Mt. Pleasant, SC). Samples were prepared in a series of digestion sets (~50 samples per set) with every 10th sample prepared in duplicate along with elemental spike recovery samples. Each set included analysis blanks, certified reference materials (UTAK) and quality control samples.

Samples (and identically treated controls) were uniformly treated with 5 mL of HNO_3 (Fisher Trace Metal Grade, Fisher Scientific, www.fishersci.com), capped and heated at 85 °C in deep cell hot blocks (Environmental Express) for 24 h. Samples were digested in capped tubes to protect from environmental background contamination and potential elemental losses from sample volatilization. Samples were cooled, then 1.5 mL of 30% H_2O_2 (Fisher Certified A.C.S., Fisher Scientific) was added to each prior to being recapped and returned to heating in the dry block at 85 °C for 8 h more. Samples were cooled, and 15 mL of 12 N HCl (Fisher Trace Metal Grade, Fisher Scientific) were added. Samples were heated at