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Blood mercury levels and fish consumption in pregnancy: Risks and benefits for birth outcomes in a prospective observational birth cohort

Caroline M Taylor*, Jean Golding, Alan M Emond

Centre for Child and Adolescent Health, School of Social and Community Medicine, University of Bristol, Bristol, UK

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ABSTRACT

Background: To avoid exposure to mercury, government advice on fish consumption during pregnancy includes information on fish species to avoid and to limit, while encouraging consumption of least two portions of fish per week. Some women may, however, chose to avoid fish completely during pregnancy despite potential benefits to the fetus.
Objectives: Our aims were to evaluate the effects of blood mercury levels in pregnant women on birth outcomes in the UK, and to compare outcomes in those who ate fish with those who did not.
Methods: Pregnant women were enrolled in the Avon Longitudinal Study of Parents and Children (ALSPAC). Whole blood samples for singleton pregnancies with a live birth were analysed for Hg by inductively coupled plasma dynamic reaction cell mass spectrometry (n = 4044). Fish intake was determined by a food frequency questionnaire during pregnancy. Data collected on the infants included anthropometric variables and gestational age at delivery. Regression models were adjusted for covariates using SPSS v23.
Results: There were no significant associations of maternal blood Hg level with birthweight, head circumference or crown–heel length in adjusted linear regression models. Similarly, there were no increased odds of low birthweight or preterm delivery in adjusted logistic regression models. When the models were repeated after stratification into fish-eaters and there were no associations except for a negative association with birthweight in non-fish-eaters (unstandardised B coefficient −58.4 (95% confidence interval −113.8, −3.0) g, p = 0.039).
Conclusion: Moderate mercury levels in pregnancy were not associated with anthropometric variables, or on the odds of low birthweight or preterm birth. Fish consumption may have a protective effect on birthweight. Consumption of fish in line with government guidelines during pregnancy should be encouraged.

1. Introduction

Mercury is a cumulative neurotoxin that is present in the environment through a variety of natural and anthropogenic sources: mercury-containing aerosols are released from volcanic activity and from the weathering of rocks, while human activities such as mining and manufacturing processes also contribute to levels in the environment (Hylander and Meili, 2003; Nriagu and Becker, 2003). Additional exposure can occur through elemental mercury vapour from dental amalgams and in some cases from the use of traditional herbal medicines and skin creams (Copan et al., 2015; Golding et al., 2013). Further exposure to mercury at a population level occurs through diet, particularly from fish that are long-lived and high in the food chain (Castano et al., 2015; Golding et al., 2013). High level exposure to mercury can result in significant neurological and behavioural disorders, including tremors, memory loss, neuromuscular changes, renal and thyroid disorders, and death; effects at more moderate levels of exposure are likely to be more subtle, and may include adverse effects on neurological function, the cardiovascular system and immune function (Karagas et al., 2012).

Mercury readily crosses the placenta and fetal levels have been found to be greater than maternal levels (Ding et al., 2013). Evidence of acute effects on the developing fetus were seen following

Abbreviations: ALSPAC, Avon Longitudinal Study of Parents and Children; B-Hg, blood mercury; B-Se, blood selenium; LBW, low birth weight; SGA, small for gestational age.

* Corresponding author. Centre for Child and Adolescent Health, School of Social and Community Medicine, Oakfield House, Oakfield Grove, University of Bristol, Bristol BS8 2BN, UK.
E-mail address: Caroline.m.taylor@bristol.ac.uk (C.M. Taylor).

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the Minamata disaster in Japan in the 1950s, in which mercury-containing by-products of a manufacturing process were released into the local bay: pregnant women who consumed contaminated seafood had a high prevalence of fetal neurotoxicity and abnormalities such as microcephaly, blindness, mental and physical disabilities (Harada, 1964). In other observational studies, detrimental effects on varied aspects of neurocognition over a range of more moderate prenatal exposure levels have been described (Jedrychowski et al., 2007; Lederman et al., 2008; Oken et al., 2008), although these findings have not always been consistent (Golding et al., 2016; Plusquellec et al., 2010).

While it is recognised that fish-eating is associated with higher levels of mercury exposure (Gundacker et al., 2010; Soon et al., 2014), fish is also an important source of several beneficial nutrients, including long-chain polyunsaturated fatty acids (particularly docosahexaenoic acid and arachidonic acid), choline, iodine, selenium and vitamin D, which are all critically important during pregnancy (Clarkson and Strain, 2003). Fish is also a major source of protein for some populations. This has resulted in a difficult task for government bodies in developing recommendations on eating fish during pregnancy, in which the beneficial effects of fish must be balanced against the potentially detrimental effects from the mercury content of different species of fish at different locations. This has resulted in somewhat confusing national advice (for example, NHS Choices (2015); US Food and Drug Administration (2004, 2014)), which may in turn result in pregnant women reducing their fish intake or avoiding it completely (Oken et al., 2003; Shimshack and Ward, 2010).

There are relatively few studies on the effect of moderate or low levels of maternal blood or cord blood/tissue mercury levels on birth outcomes such as birth weight, birth length, head circumference or gestational age (Karagas et al., 2012) (Supplementary Table A1). Such studies have generally found no associations of maternal blood mercury with these outcomes (Al-Saleh et al., 2014b; Ding et al., 2013; Gundacker et al., 2010; Lederman et al., 2008; Lucas et al., 2004; Wells et al., 2016), with a few exceptions, mainly negative associations with birthweight (Lee et al., 2010; Ramon et al., 2009). Some studies have also included data on maternal fish consumption in addition to maternal or cord blood mercury levels during pregnancy (Al-Saleh et al., 2014a; Ding et al., 2013; Gundacker et al., 2010; Lederman et al., 2008; Lee et al., 2010; Ramon et al., 2009), but few of these have stratified or adjusted for fish consumption (Al-Saleh et al., 2014a; Lederman et al., 2008; Ramon et al., 2009). These studies adjusting for fish consumption have generally shown no associations of birth outcomes with prenatal mercury exposure (Supplementary Table A1).

It has been suggested that selenium, of which fish is a rich source, may have a protective effect against the toxic effects of mercury by sequestering mercury, thus reducing its biological availability and preventing the inhibition of selenium-dependent enzymes such as glutathione peroxidase (Ralston and Raymond, 2010). This has been not been studied extensively in relation to birth outcomes, but there was little evidence for mercury–selenium interactions in association with birth outcomes in a cohort of women with moderate mercury levels (Al-Saleh et al., 2014a). This requires further investigation.

The aims of this study were to examine the associations of moderate prenatal mercury exposure in a UK population of pregnant women on birth outcomes (head circumference, crown–heel length, birth weight, low birth weight, preterm birth), and to further study associations with moderate fish-eating and blood selenium levels. An additional aim was to study associations with oily-fish-eating.

2. Methods

We first modelled associations of exposure to mercury during pregnancy using maternal blood levels during pregnancy for continuous variables (head circumference, crown–heel length, birth weight) in the newborn infant with adjusted linear regression analyses. Dichotomous variables (low birth weight and preterm delivery) were modelled with adjusted logistic regression analysis. Model 1 included adjustment for covariates such as maternal age, educational attainment, smoking and parity. Model 2 included additional adjustment for maternal blood selenium. Models 1 and 2 were repeated with stratification for fish-consumption versus non-consumption, and for oily-fish-consumption vs non-consumption.

2.1. The ALSPAC study

The sample was derived from the ALSPAC study, a population-based study investigating environmental and genetic influences on the health, behaviour and development of children. This database provided an opportunity to include a greater number of participants than has been reported on before and includes a wide range of social and demographic information to enable the most appropriate selection of covariates. All pregnant women in the former Avon Health Authority with an expected delivery date between 1 April 1991 and 31 December 1992 were eligible for the study; 14,541 pregnant women were enrolled, resulting in a cohort of 14,062 live births (Boyd et al., 2013). The social and demographic characteristics of this cohort were similar to those found in UK national census surveys (Fraser et al., 2013). Further details of ALSPAC are available at www.bris.ac.uk/alspac and the study website contains details of all the data that are available through a fully searchable data dictionary (http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary). Ethics approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees.

2.2. Collection, storage and analysis of blood samples

Whole blood samples were collected in acid-washed vacutainers (Becton and Dickinson, Oxford, UK) by midwives as early as possible in pregnancy. Whole blood samples were stored in the original tube at 4° C at the collection site before being transferred to the central Bristol laboratory within 1–4 days. Samples were at ambient temperature during transfer (up to 3 h). They were then stored at 4° C until analysis. Details of the analysis have been reported (Taylor et al., 2013). In brief, inductively-coupled plasma mass spectrometry in standard mode (R. Jones, Centers for Disease Control and Prevention (CDC), Bethesda, MD, USA CDC; Method 3009.1) was used to measure blood levels of Hg and Se with appropriate quality controls. The analyses were completed for 4134 women for Hg and 4287 for Se. One sample had an Hg level below the limit of detection: this was assigned a value of 0.7 times the lower limit of detection (LOD/$\sqrt{2}$) (Centers for Disease Control and Prevention, 2005; Hornung and Reed, 1990). No samples were below the limit of detection for Se.

2.3. Pregnancy outcomes

Newborn head circumference and crown–heel length were measured by trained study staff where the mother gave permission or if these data were missing, the values were extracted from the medical records by trained study staff. Birth weight was derived from obstetric data and from central birth notification data: where values disagreed by <100 g then the lowest value was accepted; if the values disagreed by >100 g then the value was coded as missing. Study staff were blinded to the maternal blood mercury

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