Food and Chemical Toxicology 115 (2018) 482–490

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Diet composition and serum levels of selenium species: A cross-sectional study

Tommaso Filippini[a], Bernhard Michalke[b], Lauren A. Wise[c], Carlotta Malagoli[a], Marcella Malavolti[a], Luciano Vescovi[d], Chiara Salvia[a], Annalisa Bargellini[a], Sabina Sieri[e], Vittorio Krogh[e], Margherita Ferrante[f], Marco Vinceti[a,c,*]

[a] CREAGEN, Environmental, Genetic and Nutritional Epidemiology Research Center, Section of Public Health - Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, 287 Via Campi, 41125, Modena, Italy
[b] Helmholtz Zentrum München GmbH, German Research Center for Environmental Health, Research Unit Analytical BioGeoChemistry, Ingolstädter Landstr. 1, 85764, Neuherberg, Germany
[c] Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA
[d] IREN, Reggio Emilia and Piacenza, Italy
[e] Epidemiology and Prevention Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
[f] Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", University of Catania, 87 Via S. Sofia, 95123, Catania, Italy

ARTICLE INFO

Keywords:
Selenium
Dietary intake
Food
Speciation analysis
Toxicological profile
Cross-sectional study

ABSTRACT

Selenium is a trace element of both nutritional and toxicological interest, depending on its dose and chemical form. Diet is the primary source of exposure for most individuals. We sought to investigate the influence of food intake on serum levels of selenium species.

Among fifty subjects randomly selected from a Northern Italian population, we assessed dietary habits using a validated semi-quantitative food frequency questionnaire. We also measured circulating levels of selenium species in serum using high pressure liquid chromatography associated with inductively-coupled plasma dynamic reaction cell mass spectrometer.

Circulating levels of inorganic selenium, the most toxic selenium species, were positively associated with intake of fish, legumes and dry fruits, and inversely associated with intake of dairy products and mushrooms. Concerning the organic selenium species, selenoproteinP-bound selenium was inversely associated with intake of fish, fresh fruits, vegetables, and legumes, while selenocysteine-bound selenium positively associated with intake of fresh fruit, potato, legume and mushroom. In the present study, intakes of different foods were correlated with different types of selenium species. These results have important public health implications when assessing the nutritional and toxicological potential of diet composition with reference to selenium exposure.

1. Introduction

Selenium (Se) is a metalloid considered both essential and toxic to humans, depending on the level of exposure and its specific chemical species (Fairweather-Tait et al., 2011; Jablonska and Vinceti, 2015; Vinceti et al., 2009). Its relation to human health, specifically cancer (Vinceti et al., 2016a, 2017c, 2018; Wallenberg et al., 2014), diseases of the nervous system (Cicero et al., 2017; Mandrioli et al., 2017; Vinceti et al., 2014, 2017a), and other chronic diseases (Vinceti et al., 2015b, 2016b), is still unclear, despite the large number of epidemiologic studies on the topic. Recent laboratory studies have demonstrated toxicological potential of various organic and inorganic Se species (Galant et al., 2017; Li et al., 2012; Michalke et al., 2017b; Naderi et al., 2017; Oliveira et al., 2017; Pettem et al., 2017; Rezacova et al., 2016; Selvaraj et al., 2013).

The main source of Se exposure is dietary intake (Fairweather-Tait et al., 2011; Fan and Vinceti, 2015), though occupational environment, smoking, and air pollution may also contribute to Se exposure (Jablonska and Vinceti, 2015; Vinceti et al., 2013a). Detailed studies of dietary Se intake showed that cereals, meat, fish and dairy products are the main contributors to Se dietary intake in both European and Italian populations (Filippini et al., 2018; Gudmundsdottir et al., 2012; Lombardi-Boccia et al., 2003; Mariottini et al., 1995; Navarro-Alarcon and Cabrera-Vique, 2008). The assessment of Se intake based on

* Corresponding author. CREAGEN – Section of Public Health - Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Via Campi 287, 41125 Modena, Italy.
E-mail address: marco.vinceti@unimore.it (M. Vinceti).

https://doi.org/10.1016/j.fct.2018.03.048
Received 16 January 2018; Received in revised form 14 March 2018; Accepted 30 March 2018
Available online 03 April 2018
0278-6915/

individual food consumption must consider the large variation of Se content in foods, influenced by environmental and geographic variations of Se content in soil and water (Mariottini et al., 1995; Shacklette and Boerngen, 2013), use of Se supplemented fertilizers (Fairweather-Tait et al., 2010), the differences in Se bioavailability in foods of plant origin (Baskett et al., 2001; Terry et al., 2000), and the effect of self-supplementation with Se (Satia et al., 2006).

The few observational studies investigating Se content in food and its influence on Se blood levels have considered only the total amount of the trace element (Fairweather-Tait et al., 2011; Mariottini et al., 1995; Pennington et al., 1984; Rayman, 2008), and not the single Se species. Relatively few studies have assessed the levels of Se species in biological samples, including serum, cerebrospinal fluid and urine (Combs et al., 2011; Slotnick and Nriagu, 2006; Vinceti et al., 2013b, 2015a). These studies have shown large variation in Se species levels among individuals, probably related to the variations in dietary habits (Fairweather-Tait et al., 2011). However, little is known about the Se species contained in different food items that characterize human diet, and even less about the relation between intake of specific foods and blood levels of Se species.

Recently, interest in Se speciation in foods has increased (Castro Grijalba et al., 2017; Ruiz-de-Cenzano et al., 2017), mirroring the increased attention to Se speciation in human health and disease. Distinguishing between Se species is of major relevance given the different properties of inorganic Se species, such as selenite and selenate, and of the organic forms including for instance selenomethionine (Lazard et al., 2017; Lee and Jeong, 2012; Michalke et al., 2017b; Oliveira et al., 2017; Vinceti et al., 2017b; Weekley and Harris, 2013), the markedly different and not entirely elucidated metabolism of various Se species, and the limited bioavailability of inorganic Se forms such as selenate (B'Hymer and Caruso, 2006; Gammelgaard et al., 2012; Jager et al., 2016; Weekley and Harris, 2013). The main form of Se in foods is selenomethionine (Weekley and Harris, 2013), which can be incorporated into proteins as a mimic for the correspondent sulfur-amino acid methionine (Schubert et al., 1987), a phenomenon which may cause protein misfolding and Se toxicity (Plateau et al., 2017; Vinceti et al., 2013b).

In this study, we sought to assess the influence of dietary intake on serum levels of Se species in a sample of a Northern Italian population.

2. Methods

2.1. Study population

The methodology for selection of study subjects has been described in detail elsewhere (Filippini et al., 2016; Vinceti et al., 2015a). Briefly, following approval of the study protocol by the Ethical Committee of the Policlinico University Hospital of Modena (n. 71/11), we randomly recruited fifty healthy subjects residing in Modena municipality without any relevant inflammatory disorder at the time of the recruitment, selected from sex- and age-specific subgroups through the databases of the Modena Municipality General Registry Office and using the Stata sample routine (Stata Corp., College Station, TX). Subjects were contacted from 2011 by land-line phone and invited to participate in the study. We recruited the 34% of contacted subjects and referred them to the Modena Health Unit to provide a fasting venous blood sample without any compensation apart from a complimentary breakfast.

Each participant completed a self-administered questionnaire collecting general demographic information, educational level, occupational history, smoking habits, and use of dietary supplements. In addition, we assessed their dietary habits through a validated semi-quantitative food frequency questionnaire (FFQ) specifically designed for the Central-Northern Italian population within the EPIC study (Pala et al., 2003; Pasanisi et al., 2002). A general explanation of modality of completion of the FFQ was provided to each subject soon after recruitment, and instructions were also included on the questionnaire. In addition, within each section of the questionnaire (e.g. main courses, side dishes, beverages, etc.) detailed instructions about how to answer were included. This questionnaire assessed the average frequency and amount of consumption of 188 food items over the previous year, permitting estimation of consumption of macro- and micro-nutrients (including Se). We did this using an *ad hoc* software program (Malagoli et al., 2015; Malavolti et al., 2013). In particular the estimation of Se intake was implemented through ascertainment and analysis of foods characterizing the typical Italian diet (Bottecchi and Vinceti, 2012). Food intake was reported in g/day for each food.

2.2. Laboratory analysis

Blood samples were collected in a plastic tube (BD Vacutainer®, Becton Dickinson, Milan, Italy), immediately centrifuged for 10 min at 1000 × g and serum aliquots of 1 ml were stored at −15 °C and kept continuously frozen until use. Se speciation analysis was performed at the Research Center for Environmental Health (Research Unit Analytical BioGeoChemistry, Neuherberg, Germany), using previously-described methodology (Solovyev et al., 2013; Vinceti et al., 2015a). To summarize, we slowly thawed samples in a refrigerator at 4 °C, vortexed and subsequently analyzed them. Suprapure grade chemicals were used throughout. Selenite (Se(IV)), selenate (Se(VI)), selenomethionine-bound selenium (Se-Met), selenocysteine-bound selenium (Se-Cys), thioredoxin reductase-bound selenium (Se-TXNRD), glutathione peroxidase-bound selenium (Se-GPX), human serum albumin (HSA) and Tris buffer were from Sigma-Aldrich (Deisenhofen, Germany). We purchased certified Se and Rh stock standards (1000 mg/L) from CPI International, Santa Rosa, CA, USA, and we obtained ammonium acetate (NH_4Ac) and acetic acid (HAc) from Merck, Darmstadt, Germany. $Argon_{liq}$ and methane (99.999% purity) were purchased from Air Liquide (Kleeve, Germany). We prepared stock solutions of Se(IV) and Se(VI) at a concentration of 1000 mg Se/L by dissolving in MILLI-Q water (18.2 MΩ cm, Milli-Q system, Millipore, Bedford, MA, USA). HSA was prepared at a concentration of 1000 mg/L. Preparation of Se-HSA was performed by mixing 10 mg Se/L selenite with this stock solution and incubating for at least 14 days. Working standards of Se species were prepared daily from their stock standard solutions by appropriate dilution with Milli-Q H_2O. Since selenoprotein P-bound selenium (Se-SelenoP) is not commercially available as a standard compound, it can be prepared from serum using affinity chromatography (AFC) with the methodology previously described in detail (Solovyev et al., 2013).

We determined Se species Se(IV), Se(VI), Se-Met, Se-Cys, Se-TXNRD, Se-GPX, Se-SelenoP and Se-HSA in serum samples using anion exchange chromatography (IEC) coupled with inductively-coupled plasma dynamic reaction cell mass spectrometry (ICP-DRC-MS) according to methodologies implemented for biological matrices (Michalke and Berthele, 2011; Solovyev et al., 2013). See Vinceti et al. (2015a) for the detailed experimental settings, Se species determination, and quality controls. When the concentration of a Se compound was lower than the detection limit of 0.02 μg/L, we inputted in the database half that value (0.01 μg/L) (Whitcomb and Schisterman, 2008).

2.3. Data analysis

In selecting food categories in the present study, we took into account both the typical dietary pattern of the Italian population (Turrini et al., 2001), the types of foods previously reported as being rich in Se and relevant sources of this metalloid (European Food Safety Authority, 2014; Filippini et al., 2017a, 2018), and the ability of such plants, the so called 'Se accumulator' vegetables including garlic, onion and cabbage, to accumulate large amount of the element (Finley, 2005; Terry et al., 2000). The final list of foods we selected included cereals, meat (both processed and not-processed), milk and dairy products, eggs, fish and seafood, vegetables (further divided in 'Se-accumulator' and 'Se non-