Journal of Trace Elements in Medicine and Biology 44 (2017) 322–330

Contents lists available at ScienceDirect

Journal of Trace Elements in Medicine and Biology

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

Epidemiology

Dietary and blood selenium are inversely associated with the prevalence of stroke among Inuit in Canada

Xue Feng Hu, Tasnia Sharin, Hing Man Chan*

Department of Biology, University of Ottawa, Ottawa, K1N 6N5, ON, Canada

ARTICLE INFO

Keywords:
Daily selenium intake
Whole blood selenium
Stroke
Inuit
Cross-sectional study

ABSTRACT

Inuit in Canada have high selenium intake from the consumption of country food such as fish and marine mammals. The health consequence is not known. This study examines the association between blood selenium concentration and prevalence of stroke among Canadian Inuit. The International Polar Year Inuit Health Survey was conducted in 2007–2008. Among the 2077 adults participants (≥18 years old) who completed a questionnaire and gave blood samples, 49 stroke cases were reported, 31 of which were from women. The crude prevalence of stroke was 2.4% in the participants. Participants with stroke had lower blood selenium (geometric mean: 260 μg/L vs. 319 μg/L) and dietary selenium (144 μg/day vs. 190 μg/day) compared to individuals without stroke. Participants with high blood/dietary selenium exposure (quartiles 3 and 4) had a lower prevalence of stroke compared to those with low selenium exposure (quartile 1). The adjusted odds ratio ranged from 0.09 to 0.25 among subgroups (e.g. age, sex, and blood mercury). An L-shaped relationship between prevalence of stroke with blood and dietary selenium was observed, based on the cubic restricted spline and segmented regression analyses. The estimated turning points of the L-shaped curve for blood selenium and dietary selenium were 450 μg/L and 350 μg/day, respectively. Below the turning points, it was estimated that each 50-μg/L increase in blood selenium was associated with a 38% reduction in the prevalence of stroke, and each 50-μg/day increase in dietary selenium was associated with a 30% reduction in the prevalence of stroke. In conclusion, blood and dietary selenium are reversely associated with the prevalence of stroke in Inuit, which follows an L-shaped relationship. Whether this relationship applies to other population needs further investigation.

1. Introduction

Selenium is a trace element essential to maintaining human health [1]. Selenium and selenium-dependent proteins and enzymes are involved in antioxidant defence, as well as intracellular redox regulation and modulation [2]. The relationship between selenium and cardiovascular disease is controversial. Selenium's U-shaped dose–response function on human health [3] and varied baseline selenium status among populations [4], are two plausible explanations [3]. A diet insufficient in selenium can lead to adverse effects, while exposure to too much selenium can cause toxicity. Several studies, especially from populations with low habitual selenium intake, suggest that selenium has beneficial effects on certain cancer and cardiovascular outcomes [5–9]. However, no beneficial effects on cardiovascular diseases from selenium supplement were observed in primary prevention trials conducted mainly in the US, a population with adequate dietary selenium intake [10–13]. Some studies reported that selenium was associated with increased risk of diabetes and elevated cholesterol levels [14–16], however, no or negative associations were also observed [17,18].

In the past two decades, both the age-standardized prevalence and mortality of stroke have declined in Canada as well as many other high-income countries [19,20]. However, the epidemiology of stroke and its risk factors among Inuit living in Canada is not clear. Several studies and statistics suggest that cerebrovascular disease mortality is higher among Inuit than the general populations in the United States, Canada, and Denmark [21–23]. Inuit are experiencing rapid transitions in nutrition intake and lifestyles [24]. Consequently, risk factors for stroke like obesity, diabetes, and hypertension are becoming more prevalent in Inuit communities [21,25,26]. Inuit living in Canada are exposed to high selenium levels through their traditional diet rich in marine mammals and fish [27]. Recently, a novel seleno-containing organic compound, selenoneine, showed a promising metabolic role in redox metabolites in humans [28,29]. Evidence suggests that selenoneine is present in the Arctic marine food chain, and accumulates in Inuit blood [30].

The objective of the present study was to examine the association

* Corresponding author at: Gendron Hall, 30 Marie Curie, Ottawa, ON, K1N 6N5, Canada.
E-mail address: laurie.chan@uottawa.ca (H.M. Chan).

http://dx.doi.org/10.1016/j.jtemb.2017.09.007
Received 10 July 2017; Received in revised form 1 September 2017; Accepted 5 September 2017

between dietary selenium intake from country food, blood selenium concentrations, and prevalence of stroke among Inuit living in Canada. Furthermore, we explored the potential non-linear relationship between blood/dietary selenium and prevalence of stroke.

2. Materials and methods

2.1. Study population

The International Polar Year Inuit Health Survey (IHS) was a cross-sectional survey conducted in Nunavut, Nunatsiavut, and the Inuvialuit Settlement Region in Canada in 2007 and 2008. Details of the survey have been published elsewhere [31]. Inuit adults aged 18 and older were invited to participate in the survey. Over 63% of the participants were female. A variety of topics were covered in the survey, including traditional diet and nutrition, food insecurity, chronic diseases, anthropometrics, and lab measurements of health indicators. A total of 2595 Inuit adults agreed to participate in the survey, of which 2169 completed the individual questionnaire and gave blood samples. The overall response rate was 83.6% (2169/2595).

2.2. Measurements of exposure

Dietary selenium intake from country food (i.e. dietary selenium) was estimated with a food frequency questionnaire, the details of which have been published elsewhere [27]. The food frequency questionnaire only examined country food. Country food is the name that Inuit use to describe traditional foods harvested locally, e.g. arctic char, seal meat, whale, and caribou. The list of country foods included in the questionnaire was based on a revised version of the Centre for Indigenous Peoples' Nutrition and Environments' Inuit traditional food frequency questionnaire [27]. Whole blood selenium concentration was used as another exposure indicator. Details of the analytic methods and quality control procedures have been described in detail previously [27,32]. Fasted blood samples (at least eight hours, not no more than 16 h) were collected in plastic BD Vacutainer tubes (Becton Dickinson and Company, Franklin Lakes, NJ) coated with K_2EDTA for whole blood and stored at −80 °C until analysis. Samples were analyzed at the Laboratoire de Toxicologie, Institut National de Santé Publique (Québec, QC, Canada), [ISO (International Organization for Standardization) accreditation 17025], which participates in the quality-assurance quality-control programs of the German External Quality Assessment Scheme and the Quebec Multi-element External Quality Assessment Scheme. An Elan DRC II (Perkin-Elmer) inductively coupled plasma mass spectrometer was used to measure selenium in whole blood [27,32]. The limit of detection was 0.21 nmol/L, and the reproducibility was 3.8%. The blood selenium concentration was converted into microgram/litre (μg/L) and log-transformed, because the selenium distribution was skewed positively. Dietary selenium was expressed as the average daily intake (μg/day). Participants were divided into quartiles according to dietary/blood selenium, and the first quartile was used as the reference category.

2.3. Measurements of outcomes and confounders

The occurrence of stroke was recorded using self-disclosure of physician-diagnosed stroke. Participants were asked, "Did a doctor or a nurse ever tell you that you suffered from stroke?" A total of 2077 valid answers were recorded, along with information on known risk factors. Parents' history of stroke was defined as either parent being diagnosed with a stroke. Systolic and diastolic blood pressure measurements were calculated from the average of three readings. Blood cholesterol and glucose concentrations were measured after 8 h but no more than 16 h of fasting. BMI was calculated by dividing the weight by the square of height. Total omega-3 fatty acids were measured in red blood cell (RBC) membranes and expressed as a percentage of weight (wt%) to total fatty acids identified [33]. Total blood mercury was measured following the same procedure as that of selenium. In addition, blood plasma concentrations of polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) were measured [32]. Diabetes was defined as either self-reported of physician-diagnosed diabetes, fasting plasma glucose ≥7.0 mmol/L, oral glucose tolerance test ≥11.1 mmol/L, or currently on diabetes medication. Finally, the survey measured physical inactivity, which was defined as average moderate-intensity physical activity < 150 min in a week.

2.4. Statistical analysis

The characteristics of the participants were assessed with descriptive statistics, including frequency, mean, and standard deviation. In this study, we investigated the association between dietary/blood selenium and prevalence of stroke following three steps. First, we examined the dietary/blood selenium difference by stroke status. The age- and sex-adjusted arithmetic mean (AM) for dietary selenium and geometric mean (GM) for blood selenium were calculated using a general linear model. Second, we used unconditional logistic regressions to investigate the difference in prevalence of stroke by dietary/blood selenium quartiles, adjusting for age, sex, systolic blood pressure, smoking status, total cholesterol, diabetes, and parents' history of stroke. Both analyses were stratified by variables in which either the prevalence of stroke or blood/dietary selenium were not evenly distributed: sex, age (< 40 and ≥40 years old), education (primary, secondary, and higher), total omega-3 fatty acids (< 5.4 and ≥5.4 wt% of total fatty acids), and blood mercury concentration (< 7.8 and ≥7.8 μg/L). The cut-offs were the medians of the variables of interest (e.g. the median of mercury concentration was 7.8 μg/L). The adjusted odds ratios (ORs) of the prevalence of stroke by dietary/blood selenium quartiles, as obtained from the logistic regressions, were visually depicted in a forest plot.

Third, two further efforts were made to quantify the potential non-linear association between selenium and stroke. Restricted cubic spline regression (RCS) was fitted for dietary/blood selenium to examine the shape of the dose–response curve [34]. Segmented logistic regression, with two breakpoints, was fitted to examine if the association between dietary/blood selenium and prevalence of stroke changed at different doses, and to check whether the breakpoints identified were in accordance with the RCS results[35]. The adjusted ORs associated with each increase of 50 μg/L in blood selenium or 50 μg/day in dietary selenium were reported for ease of interpretation. A forward procedure was adopted to show the relative contribution of other risk factors and their influence on selenium's effect size and the breakpoints. Model 1 included selenium, age, and sex; Model 2 added traditional stroke risk factors (smoking, diabetes, systolic blood pressure, total cholesterol, BMI, physical inactivity, and parents' history of stroke); Model 3 added socioeconomic status (education, marital status, occupation, and personal income); Model 4 added omega-3 fatty acid composition, mercury, sum of PCBs, and sum of PBDEs. Medication information was not controlled in the model as it was not clear for primary prevention or secondary prevention of stroke. Marine mammals and fish intake were not controlled as they are in the same causal pathway between selenium and stroke. The descriptive analysis, logistic regressions, and forest plot were performed with Stata version 14.1 (StataCorp LP, College Station, TX, USA), while the RCS and segmented logistic regression were performed with R (R Core Development Team).

3. Results

The characteristics of the participants are shown in Table 1. The mean age of the participants was 42 years, and over 60% of the participants were female. Among the participants, 70% were current smokers. A total of 49 stroke cases were identified, accounting for 2.36% of the total participants. People with stroke were older (by 8 years on