Archives of Gerontology and Geriatrics 60 (2015) 147–152

Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

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

The association between selenium and lipid levels: A longitudinal study in rural elderly Chinese

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ARTICLE INFO

Article history:
Received 23 January 2014
Received in revised form 10 September 2014
Accepted 11 September 2014
Available online 22 September 2014

Keywords:
Selenium
Lipids
Elderly Chinese

ABSTRACT

Objective: A protective effect of selenium on lipid levels has been reported in populations with relatively low selenium status. However, recent studies found that high selenium exposure may lead to adverse cardiometabolic effects, particularly in selenium-replete populations. We examined the associations of selenium status with changes in lipid levels in a 7-year follow up of an elderly Chinese cohort including participants from selenium-deplete areas.

Methods: Study population consisted of 140 elderly Chinese aged 65 or older with nail selenium levels measured at baseline (2003–2005). Lipid concentrations were measured in fasting blood samples collected at baseline and the 7-year follow-up (2010–2012). Analysis of covariance (ANCOVA) models was used to determine the association between baseline selenium status and changes in lipid levels from baseline to follow-up adjusting for other covariates.

Results: Mean (±standard deviation) baseline selenium concentration was 0.41 ± 0.2 mg/kg. In prospective analysis, we found that individuals in the highest selenium quartile group showed 1.11 SD decrease on total-cholesterol ($p < 0.001$), 0.41 SD increase on HDL-cholesterol ($p < 0.001$) and 0.52 SD decrease on triglyceride after 7 years than those in the lowest selenium quartile group. The similar trends were seen with significant lipid changes in the 2nd and 3rd quartile groups.

Conclusion: Selenium has modest beneficial effects on blood lipid levels in a population with relatively low selenium status. Our result suggests adequate dietary selenium intake as a potential prevention strategy for lowering lipid levels in selenium deplete populations.

1. Introduction

Selenium is an essential micronutrient with a narrow safety margin. Adequate selenium intake is needed to maximize antioxidant activities of glutathione peroxidases and other selenoproteins (Panel on Dietary Antioxidants and Related Compounds et al., 2000; Rayman, 2000). In animal experiments, selenium supplementation decreased plasma total and low-density lipoprotein cholesterol levels and increased HDL cholesterol levels, whereas selenium deficiency had the opposite effect (Mazur et al., 1996; Wójcicki et al., 1991; Wolf et al., 2010). However, the relationship between selenium status and cardiovascular disease risk in human studies remains inconsistent (Bjelakovic, Nikolova, Gluud, Simonetti, & Gluud, 2007; Flores-Mateo, Navas-Acien, Pastor-Barriuso, & Guallar, 2006; Stranges et al., 2006; Stranges, Navas-Acien, Rayman, & Guallar, 2010).

Several cross-sectional studies have examined the association between selenium levels and lipids profile (Berr et al., 1998; Jossa et al., 1991; Laclaustra, Stranges, Navas-Acien, Ordovas, & Guallar, 2009; Ringstad, Jacobsen, & Thomassen, 1987; Stranges, Laclaustra, et al., 2010; Yang et al., 2010), or between selenium levels and the risk of cardiovascular diseases (CVD) (Bjelakovic et al., 2007; Bleys, Navas-Acien, & Guallar, 2008; Bleys et al., 2009; Flores-Mateo et al., 2006; Salonen, Alfthan, Huttunen, Pikkarainen, & Puska, 1982;

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http://dx.doi.org/10.1016/j.archger.2014.09.005
0167-4943/

Stranges et al., 2006; Stranges, Navas-Acien, et al., 2010; Suadicani, Hein, & Gyntelberg, 1992; Virtamo et al., 1985; Wei et al., 2004) in different populations. An association between higher selenium level and lower lipids has been reported particularly in populations with relatively low selenium status (Flores-Mateo et al., 2006; Salonen et al., 1982; Virtamo et al., 1985; Wei et al., 2004). However, in contrast to the putative benefits of selenium, recent observational studies have raised concern that high selenium exposure may lead to adverse cardiometabolic effects, particularly in selenium replete populations such as that of the US (Laclaustra, Navas-Acien, Stranges, Ordovas, & Guallar, 2009; Laclaustra et al., 2010; Stranges et al., 2007; Stranges, Laclaustra, et al., 2010). Furthermore, a few randomized trials found no effect of selenium supplementation on serum cholesterol level (Yu et al., 1990) and cardiovascular disease prevention (Stranges et al., 2006). Nonetheless, most of these studies are cross-sectional, which cannot establish a causality relationship, and there is little longitudinal data on the relationship between selenium status and lipids profiles of the elderly.

Data from our populations where selenium supplementation is rare may be able to offer insight on the relationship between selenium and lipid levels. In this article, we report results from a longitudinal study of rural elderly Chinese cohort and examine the association between baseline selenium status and changes in lipid levels.

2. Methods

2.1. Study population

Participants for the current study were from the Selenium and Cognitive Decline study, a longitudinal epidemiologic project funded by the National Institute of Health examining the long-term impact of selenium on cognitive decline in rural elderly Chinese. Two thousand Chinese aged 65 and older from four counties in China were enrolled at baseline between December 2003 and May 2005. Details of the study and its methodological procedures have been previously described (Gao et al., 2007; Gao et al., 2008). At baseline, venous blood samples were collected after the subjects had fasted for at least 12 h from 10% of participants from each county (n = 199); of these, 140 subjects were seen again in 2010–2012 and a second fasting blood sample was collected. Approximately 23.6% were lost among the two thousand participants between baseline and the seven years follow-up, but the characteristics of those lost were not significantly different from subjects with followed-up (data not shown). The Indiana University institutional review board and the Institute for Environmental Health and Related Product Safety, Chinese Center for Disease Control and Prevention approved the study.

2.2. Selenium measures

At baseline, nail samples from all study subjects were collected at the time of interview and stored in clean plastic bags labeled with subject identification numbers. Fluorometric determination of trace amount of selenium with 2,3-diaminonaphthalene, described in details elsewhere (Li, Cao, & Sun, 1991), was used to determine trace amounts of selenium in nail samples. Quality control measures in the laboratory were described previously (Gao et al., 2007).

2.3. Lipids measurements

At both baseline and follow-up examination, serum total cholesterol, high-density lipoprotein (HDL) and triglyceride were tested by Roche Diagnostic kits (enzymic colorimetric method), using Hitachi 7180 automatic biochemistry analyzer. In addition to quality control samples, duplicate samples were used in the lab analysis. If the relative deviation of parallel samples was greater than 10%, we repeated measurement. The average of the two measurements was used in all analyses. The intra- and inter-assay coefficients of variation were less than 1.2% for total cholesterol, 0.9% for HDL cholesterol and 1.4% for triglyceride levels.

2.4. Other information

Other information collected during the baseline interview included age, gender, years of education, body mass index (BMI), whether a participant is a life-long resident of the village since birth, history of alcohol and smoking, and self-reported history of stroke, hypertension, and heart attack. BMI (defined as body weight in kilograms divided by height in meters squared) was derived from height and weight measurements.

2.5. Statistical analysis

Descriptive data are expressed as means and standard deviation, or as percentages. Paired t-tests were used to detect significant change in cholesterol, HDL and triglyceride levels from baseline to 7-year follow-up. To detect potential non-linear relationship between selenium and lipid levels, participants were divided into quartile groups according to baseline selenium concentrations. Analysis of variance (ANOVA) was used to compare differences among group means, and chi-squared tests were used for differences in proportions between categorical variables.

For each participant with follow-up evaluation, changes in lipid levels were derived as the difference between follow-up and baseline measures. ANCOVA models was used to determine the association between baseline selenium quartile groups and changes in lipid level while adjusting for covariates. Separate ANCOVA models were used for cholesterol, HDL and triglyceride, respectively.

3. Results

Table 1 shows the baseline characteristics of the study population by quartiles of baseline nail selenium concentrations. In the 140 participants, mean (SD) nail selenium concentrations were 0.41 (0.2) mg/kg, and mean (SD) cholesterol, HDL and triglyceride concentrations were 4.00 (0.8), 1.15 (0.3), and 1.11 (0.3) (mmol/L), respectively. Higher selenium concentrations were associated with higher BMI, and higher systolic blood pressure measures. Age, sex, life-long residency, history of smoking and drinking alcohol, and other self-reported diseases history did not differ significantly across the selenium quartile groups. Among the baseline participants, selenium concentrations were inversely correlated with HDL ($r = -0.21$, $p = 0.02$).

For the 140 participants who had 7-year follow-up evaluations, triglyceride level had decreased significantly at follow-up ($p = 0.003$). The Pearson correlation coefficients between baseline and follow-up levels were 0.267, 0.395, and 0.456 for cholesterol, HDL, and triglyceride respectively ($p < 0.001$ for all) (see Table 2).

Results from separate ANCOVA models presented in Table 3 showed that baseline selenium level was a strong predictor of the changes of serum total cholesterol ($p < 0.001$), HDL-cholesterol ($p < 0.001$) and triglyceride ($p = 0.015$) between follow-up and baseline measures, after adjustment for BMI, systolic blood pressure and other covariates. Participants in the bottom selenium quartile group were used as the reference group in all models. Individuals in the highest selenium quartile group showed 1.11 SD decrease on total-cholesterol ($p < 0.001$), 0.41 SD increase on HDL-cholesterol ($p < 0.001$) and 0.52 SD decrease on triglyceride after 7 years than those in the lowest selenium quartile group. The same trends were seen with significant changes in lipids in the 2nd and