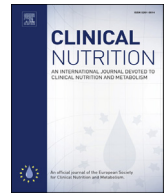




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Original article

Relationship between higher serum selenium level and adverse blood lipid profile

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SUMMARY

Background: As the key component of glutathione peroxidase with unique antioxidant properties, selenium has been considered to play an important part on lipid metabolism. However, the associations of serum selenium concentrations with lipid concentrations and dyslipidemia are still controversial.

Methods: We analyzed cross-sectional data including serum selenium levels, lipid concentrations and other related indexes of 8198 rural Chinese. Serum selenium was measured by inductively coupled plasma mass spectrometry, and total cholesterol (TC), triglyceride (TG), high density lipoprotein-cholesterol (HDL-c) and low density lipoprotein-cholesterol (LDL-c) of serum were measured with kits. **Results:** Overall, mean serum selenium was 120 µg/l. Multivariate linear regression revealed that selenium concentrations were positively correlated with TC ($P < 0.001$), HDL-c ($P < 0.001$), TG ($P < 0.001$) and LDL-c ($P < 0.001$). Compared with the lowest quintile of serum selenium, participants in quintile 3, 4 and 5 had higher risks of High-TC dyslipidemia ($P \leq 0.02$) and High-LDL-c dyslipidemia ($P < 0.02$) after adjusting for covariates. In the stratified analyses, we found that the selenium–dyslipidemia associations were significantly stronger in post-menopausal women (OR: 2.72; 95% CI: 1.97, 4.17) and diabetics (OR: 9.40; 95% CI: 3.02, 29.26).

Conclusion: Elevated serum selenium levels were correlated with the increased concentrations of TC, LDL-c, HDL-c and TG, and increased the risk of High-TC and High-LDL-c dyslipidemia among rural Chinese. However, the real associations between serum selenium and lipid profile should be verified in specifically designed randomized trials in future.

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1. Introduction

Selenium (Se), as an essential microelement, is considered to have beneficial effect on human health, mainly based on the antioxidant capacity of glutathione peroxidases (GPx) and other selenoproteins involved in essential enzymatic functions, such as redox homeostasis, thyroid hormone metabolism, and reproduction [1,2]. A wide range of dietary selenium sources comprises meat, guts, seafood, and cereals. Recommended Dietary Allowance for selenium (55 µg/d) is crucial for maintaining the function and homeostasis of the human body. Selenium levels in people vary widely. Published studies showed that the mean serum selenium

levels were ranging from 51.8 to 142.9 µg/l among people in Britain, Canada, Finland, Germany, South Africa and USA [3–8].

Previous epidemiological researches revealed that the correlation between serum selenium levels and cardiovascular diseases was inconsistent. Studies from Germany [6] and Denmark [9] showed that reduced selenium levels could be one of the risk factors for cardiovascular diseases (CVD). A follow-up study among Italian [10] corroborated high selenium levels with dyslipidemia and diabetes. However, some studies have been unable to demonstrate a correlation of serum selenium with the risk of CVD [11–13]. As a modifiable risk factor of CVD, dyslipidemia, which is characterized by abnormal levels of circulating lipids and lipoproteins, can be divided into four common types, high total cholesterol (TC) dyslipidemia (TC > 5.17 mmol/l), high low density lipoprotein (LDL) cholesterol dyslipidemia (LDL-c > 3.36 mmol/l), high triglycerides (TG) dyslipidemia (TG > 1.69 mmol/l), and low high density lipoprotein (HDL) cholesterol dyslipidemia (HDL-c < 1.04 mmol/l)

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according to Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults [14].

As the crucial component of GPx with unique antioxidant properties, selenium has been regarded as one of the important factors for lipid metabolism [15]. However, an increased risk of dyslipidemia in people with high selenium exposure has been observed in recent researches. Observational studies have revealed that serum selenium was positively correlated with LDL-c [8,16–18], TC [3,8,16–18], or TG [8]. However, randomized controlled trials (RCTs) on the effect of selenium supplementation on lipid concentrations are limited to studies in which selenium supplements were given combined with other minerals or to small short-term studies, and results of RCTs didn't find significant association between serum selenium and lipid profile [19–21].

China has a large proportion of agriculture and rural people. Rural Chinese usually eat locally produced food, and seldom eat any dietary supplements. In addition, most of them are local inhabitants at the same place during their lifetime [22]. So it is of great significance to probe into the correlations between serum selenium concentrations and lipid or dyslipidemia in rural Chinese. To our knowledge, there were few large-scale studies conducted in China to evaluate the correlations between serum selenium levels and lipid concentrations. Su et al. found that high selenium level in nail could increase the risk of dyslipidemia [23]. A study [24] from Zhoukoudian area, Beijing in 2007 revealed that selenium concentrations were positively correlated with TC, and negatively correlated with TG and HDL-c. However, the final result may be limited to the small sample size.

Our objective in the cross-sectional study, therefore, was to explore the associations between serum selenium levels and lipid concentrations, and further investigated the effect of selenium status on the risk of dyslipidemia among participants over eighteen from rural areas in China.

2. Methods

2.1. Study population

The study population of our study was from Shandong University health research base, a cohort study on participants from rural areas in three counties (Junan, Liangshan and Pingyin) of Shandong Province in China. We excluded population under 18 years old and people with missing data on selenium, and the final sample size was 8198. All people involved in this study obtained written informed consent before collecting blood samples.

2.2. Examination of blood biochemical indicators

Fasting serum TC, TG, LDL-c, HDL-c, plasma glucose, serum selenium were determined with the morning fasting venous blood. Serum samples were centrifuged with 1000 rpm for 5–10 min after placing at room temperature for 30 min, then draw the upper layer of serum into the centrifuge tube. All blood samples were kept in –80 °C refrigerator until analysis. Blood glucose was determined by Glucose Oxidase method, and used the blood glucose Kit in fully automatic chemistry analyzer. Serum selenium was determined by inductively coupled plasma mass spectrometry. TC, TG, HDL-c and LDL-c of serum were measured with TC kit, TG kit, HDL-c kit, and LDL-c kit.

2.3. Other variables

Age, gender, current cigarette smoking (yes, no), current alcohol use (yes, no), cardiovascular diseases (yes, no), family history of cardiovascular diseases (yes, no) and static activities (h) were self-

reported. We used traditional methods to measure height, weight, and blood pressure (BP). The average values of the two measurements were obtained, and the results were accurate to 0.1 cm, 0.1 kg, 1 mmHg. Hypertension was defined as systolic blood pressure > 140 mmHg and/or diastolic blood pressure > 90 mmHg. The dietary pattern and nutritional status of participants were investigated by 24 h dietary investigation inquiring for three days.

2.4. Statistical analysis

Participants were divided into quintiles by serum selenium concentration, and participants in the lowest quintiles were chosen as the reference group. Measurement data are expressed as the mean ± standard deviation (SD), and dichotomous variables were expressed as percentages. We estimated the differences in the levels of TC, TG, LDL-c, and HDL-c by multivariate linear regression, and calculated the odds ratios (OR) and 95% confidence intervals (CI) for 4 kinds of dyslipidemia by logistic regression, comparing the 4 higher quintiles to the lowest quintile. We used three models with progressive degrees of adjustment. Model 1 was adjusted for sex (male, female), age. Model 2 was further adjusted for BMI, hypertension (yes, no), diabetes (yes, no), family history of CVD (yes, no), current cigarette smoking (yes, no), current alcohol use (yes, no) and static activities time. Model 3 was further adjusted for the dietary intakes of energy, fat, vitamins E, calcium, and magnesium. Moreover, we estimated the correlation between serum selenium level and dyslipidemia (including four types) by performing analyses in which people were stratified according to covariates, including age (<40, 40–60, >60), gender (male, pre-menopausal women, post-menopausal women), current smoking status (yes, no), current alcohol use (yes, no), diabetes (yes, no), hypertension (yes, no) with Model 3 adjustment. All analyses were performed with using the SPSS statistical software version 23.0.

3. Result

3.1. Baseline clinical characteristics

A total of 8198 participants aged from 18 to 95 were included in our cross-sectional analysis at baseline. Table 1 describes the general characteristics of the people involved in our study across quintile categories of plasma selenium. Mean concentration of selenium in the general population was 120 µg/l. Mean serum selenium concentration of each quintile group was 80.87 µg/l, 101.78 µg/l, 116.36 µg/l, 132.60 µg/l, 168.51 µg/l. Higher selenium was correlated with higher age, higher BMI, higher BP, higher blood glucose, smoking status, drinking status, lower static activities time and higher fat intakes from dietary.

3.2. Relationships between serum selenium and lipid profile

In multivariate liner regression analysis, high serum selenium levels were associated with higher level of TC, TG, LDL-c, and HDL-c. The multivariable-adjusted differences in TG, TC, LDL-c, and HDL-c were 0.24 mmol/l (95% CI: 0.17, 0.31), 0.57 mmol/l (95% CI: 0.49, 0.65), 0.37 mmol/l (95% CI: 0.32, 0.42), and 0.12 mmol/l (95% CI: 0.08, 0.16), respectively (Table 2).

3.3. Relationships between serum selenium and dyslipidemia

Table 3 revealed positive associations of serum selenium concentrations with High-TC and High-LDLC dyslipidemia after adjusting the age and sex, and adjustment for lifestyle and dietary factors only slightly attenuated these associations. Multivariable-adjusted OR in High-TC dyslipidemia comparing quintiles 3–5 to

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