Effect of selenium supplementation on plasma lipid and lipoprotein cholesterol levels in adult rats

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ABSTRACT
Objectives: Selenium is an antioxidant nutrient that prevents lipid peroxidation. The objective of the study was to investigate long-term effects of selenium supplementation on plasma lipid profile in rats. Design: To investigate the effect of this micronutrient on plasma lipid levels, adult rats supplemented with selenium (20 μg/Kg body weight) for 16 weeks were studied. Plasma selenium levels were found to be 167.9 ± 4.8 μg/l and 193.9 ± 3.8 μg/l in control and selenium treated rats, respectively. Results: Selenium supplementation significantly lowered the concentrations of plasma triglycerides by 21% and low density lipoprotein cholesterol (LDL-cho) by 42%. Also, the ratio of LDL-cho to either high density lipoprotein cholesterol (HDL-cho) or to total-cho was significantly lowered. On the other hand, selenium did not influence HDL-cho and total-cho concentrations. Moreover, H/LD ratio was significantly increased (p<0.001). Plasma selenium levels in the examined rats were negatively correlated with plasma triglycerides (r = -0.3479) and LDL-cho (r = -0.3177) concentrations. Conclusions: Therefore, the food supplementation with selenium might be beneficial in improving lipid profile, the major risk factor for coronary heart disease (CHD).

Keywords: Selenium, antiatherosclerotic, lipid, lipoprotein-cholesterol, rats.

Lipoproteins, particularly low density lipoprotein cholesterol (LDL-cho), have relevance mainly for development of atherosclerosis. Oxidative modifications of LDL increases its atherogenicity and has been suggested to have a major role in the progression of atherosclerosis. Selenium is an antioxidant nutrient that inhibits in vivo lipid peroxidation and, therefore, inhibits the oxidative modification of LDL. Despite the potential importance of selenium in preventing lipid peroxidation, there are few nutritional studies focusing on the overall influence of this micronutrient on lipid and lipoprotein metabolism. Most of these reports investigated the relationship between selenium deficiency and fatty acid changes and their association with coronary heart disease (CHD). Moreover, the articles which investigated the effect of this micronutrient on lipoprotein metabolism tested the relation between selenium deficiency and the development of atherosclerosis in humans. It becomes tempting to see if selenium supplementation has the potential to modify lipid profile in normal states. Therefore, the present experiment was designed to study plasma lipid and lipoprotein-cholesterol changes in adult rats kept on selenium supplementation for 16 weeks in a trial to test the possibility of using this micronutrient as an adjuvant to keep better plasma lipid levels in healthy subjects.

Methods: Adult Wistar albino rats of both sexes, weighing 200 ± 50 g were used. Rats were individually housed in a room kept at 22°C with a 14:10 h light/dark cycle and provided with standard rat chow and water ad libitum. Rats were randomly divided into 2 groups, selenium treated (n = 14) and control (n = 15) rats. The selenium group received through gavage feeding a daily oral dose of selenium methionate 20 μg/kg body weight. This dose of selenium is nutritionally nontoxic according to the report of US NAS/NRC in 1971. Control rats were sham fed (by substituting distilled water for selenium methionate) so that animals would be handled in the same manner. After 16 weeks of treatment, fasted animals (16 h) were weighed, anesthetized with sodium...
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Table 1 - Body weight gain and plasma selenium, triglycerides and total cholesterol levels of adult rats fed standard diet alone or supplemented with selenium.

<table>
<thead>
<tr>
<th>Dietary group*</th>
<th>Test Parameters (means ± SEM)</th>
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<tr>
<td></td>
<td>Weight gain (g)</td>
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<tr>
<td>Control (15 rats)</td>
<td>94.6 ± 9.3</td>
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<tr>
<td>Selenium treated (14 rats)</td>
<td>102.7 ± 3.6</td>
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* Measurements were made after 16 weeks of treatment
  a significantly different from control at p < 0.001
  b significantly different from control at p < 0.05

pentobarbital (40 mg/kg body weight, i.p.) and blood was withdrawn from the abdominal aorta into chilled heparinized tubes. Plasma samples were separated by centrifugation at 3000 r.p.m. for 20 minutes and stored at -20 °C until assayed.

All plasma samples were subjected to enzymatic colormetric assays that were previously described for determination of plasma triglycerides,¹¹ total cholesterol¹² and high density lipoprotein cholesterol¹³ using kits supplied by Boehringer Mannheim. Low density lipoprotein cholesterol was calculated by a method previously described.¹⁴ Plasma selenium level was measured, using Perkin Elmer 460 atomic absorption spectrophotometer, according to the method of Tulley and Lehmann.¹⁵

Results were presented as mean ± standard error of the mean (SEM). Statistical analysis was performed by Student's t-test (unpaired)¹⁶ at a level of significance of <0.05 and correlation were computed using linear regression analysis by the least squares method.¹⁷

Results Body weight gain and plasma selenium, triglycerides and total cholesterol concentrations of control and selenium fed rats are summarized in Table 1. Following 16 weeks of treatment the average plasma selenium level was 193.9 ± 3.8 µg/l (= 2.45 µmol/l) in selenium fed rats and 167.9 ± 48 µg/l (= 2.12 µmol/l) in control rats. The mean body weight gain of both groups, as seen in Table 1, was not significantly different (p>0.05). Also, total plasma cholesterol concentrations in selenium fed rats showed insignificant low values when compared to rats fed basal diet (p>0.05). On the other hand, selenium induced significant decline in serum triglyceride concentrations (by 21%, p<0.05) compared to control rats.

Plasma low density lipoprotein cholesterol (LDL-cho) and high density lipoprotein cholesterol (HDL-cho) concentrations as well as LDL-cho/HDL-cho, LDL-cho/total-cho and HDL-cho/total-cho ratios in the examined rats are illustrated in Table 2. As noted from Table 2, selenium supplementation induced significant lowering in plasma LDL-cho (p<0.05) to reach values about 58% of that found in rats fed basal diet. Additionally, selenium induced significant decline in LDL-cho/HDL-cho and LDL-cho/total-cho ratios (p<0.001).

| Table 2 - Plasma LDL and HDL cholesterol concentrations and LDL-cho/HDL-cho, LDL-cho/total-cho and HDL-cho/total-cho ratios in adult rats fed standard diet alone or supplemented with selenium. |
|-------------------------|-------------------------------|
|                         | Test Parameters (means ± SEM) |
|                         | LDL-Cholesterol (mg/dl) | HDL-Cholesterol (mg/dl) | LDL-cho/HDL-cho ratio | LDL-cho/total-cho ratio | HDL-cho/total-cho ratio |
| Control (15 rats)       | 13.13 ± 1.29               | 44.45 ± 2.05             | 0.30 ± 0.03            | 0.19 ± 0.02             | 0.63 ± 0.02             |
| Selenium treated (14 rats) | 7.64 ± 1.16*               | 46.7 ± 3.19              | 0.18 ± 0.03*           | 0.12 ± 0.02*           | 0.72 ± 0.02*           |

*Measurements were made after 16 weeks of treatment
  aSignificantly different from control at p<0.05
  bSignificantly different from control at p<0.001
cho ratios (p<0.05) when compared to control group. Meanwhile, significant increment in HDL-cho/total-cho ratio (p<0.001) was detected in selenium fed rats. HDL-cho concentrations were comparable in both examined groups and no significant differences were observed between rats (p>0.05).

Plasma selenium (Figs. 1,2) in the examined rats is inversely correlated with plasma triglycerides (r = 0.3479, n = 29, p<0.01) and LDL-cho (r = 0.3117, n = 29, p<0.05). No such correlation was found between plasma selenium and either plasma cholesterol or plasma HDL-cho levels.

Discussion

The present investigation showed that selenium has the potential to improve lipid profile, the major risk factor in CHD. Selenium administration for 16 weeks significantly lowered plasma triglyceride (by 42%) and LDL-cho (by 21%) concentrations. Selenium also altered the ratios between different lipoprotein fractions so that LDL-cho/HDL-cho and LDL-cho/total-cho were significantly decreased and HDL-cho/total-cho was significantly increased when rats supplemented with this micronutrient.

Reports showed that selenium could improve the dyslipidemia induced by dietary manipulation. Marked suppression of triglycerides and total cholesterol were observed when rabbits were fed with a high fat diet supplemented with selenium. Interestingly, the present data showed that feeding rats selenium with basal diet also lowered plasma triglycerides significantly and tended to decrease total cholesterol levels. Furthermore a detected inverse correlation between plasma selenium and triglyceride levels was observed in the examined rats. Unfortunately the available previous reports on rats were devoid of such correlation. On the contrary, human study revealed a strong direct linear correlation between plasma selenium and triglycerides and plasma selenium and cholesterol in healthy children. Disturbed lipoprotein profile is a major contributing cause of CHD. Raised circulating LDL-cho level was assumed to be necessary for the development of atherosclerosis. Besides, lowered LDL-cho/HDL-cho and elevated HDL-cho/total-cho ratios were found to be strong negative indices for atherosclerosis risk. The current results, in support of opinion of others, showed that selenium is an effective antiatherogenic micronutrient because of its marked lowering effect on LDL-cho level. Not only raising of plasma selenium concentration by 15% induced 42% decline in LDL-cho but also an inverse linear correlation between plasma selenium level and LDL-cho was observed. Additionally ratios between lipoprotein fractions were modified by selenium supplementation and about 40% reduction in LDL-cho/HDL-cho and 12% elevation in HDL-cho/total-cho were found in selenium fed rats. Consistently, Stone et al. reported that selenium deficiency alone was primarily responsible for raising LDL-cho levels in normal and spontaneous hypertensive rats. Also their experiment showed that selenium induced marked reduction in LDL-cho/HDL-cho ratio.

The mechanism through which selenium modified cholesterol distribution in lipoprotein fractions is unknown. Plasma LDL-cho concentration is regulated by rate of synthesis and the efficiency of catabolism via high affinity receptor mechanisms. One explanation for selenium induced decline in LDL-cho could be increased peripheral catabolism. The oxidatively modified LDL has an altered receptor mediated catabolism and was suggested to be the cause for decreased rate of removal of LDL. Therefore, selenium being an antioxidant could prevent such alteration in LDL catabolism. Alternatively, selenium could decrease plasma LDL level by modifying hepatic synthesis and secretion of its...
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precursor very low density lipoprotein (VLDL). Stone et al strongly supports such a proposal as they found livers from rats fed selenium deficient diet secreted more VLDL. Probably the obtained low triglyceride levels here in selenium treated rats support this opinion since VLDL is the main carrier for triglycerides in fasting states (16 h fast). Therefore, more than one mechanism may play a role in selenium induced lipoprotein alterations.

Conclusion The present work draws the attention to selenium as a selectively effective micronutrient in lowering LDL-cho, besides its known importance of being an antioxidant.

References


