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Serum Selenium is Related to Low-density Lipoproteins in Healthy Children But Not in Children With Diabetes

Mehari Gebre-Medhin, Uwe Ewald and Torsten Tuvemo
Department of Pediatrics, University Hospital, Uppsala, Sweden

ABSTRACT

The serum concentrations of selenium in 13 healthy children and 27 children with type 1 diabetes mellitus were evaluated in relation to serum lipoprotein and apolipoprotein concentrations. In healthy children a correlation was found between serum selenium and both serum cholesterol ($r=0.56$; $p<0.05$) and serum triglycerides ($r=0.56$; <0.05) and their low-density lipoprotein (LDL) + very low-density lipoprotein (VLDL) fractions ($r=0.60$ and 0.56 respectively; $p<0.05$), but not their high-density lipoprotein fractions. Associations were also found between selenium and apolipoproteins, especially A II and C II ($r=0.57$; $p<0.05$).

In diabetic children serum selenium was significantly correlated with apolipoproteins A II and Apo C II, but not with any lipoprotein or lipid or any of their fractions.

This study supports the hypothesis that serum selenium is an integral part of the defence system against degradation products associated with LDL and VLDL in young healthy humans. These associations were not found in diabetes, which might suggest that the defence system against lipid peroxidation is less effective in this disease.

INTRODUCTION

Selenium is an integral part of the erythrocyte enzyme glutathione peroxidase (GSH-Px) (12). This enzyme is involved in the destruction of toxic lipid peroxides and selenium is thus regarded, together with vitamin E, as part of the defence mechanism against the biological effects of free oxygen radicals and lipid peroxidation. It has recently been suggested that one of the mechanisms underlying the augmented risk of atherosclerosis in patients with elevated serum levels of low-density lipoprotein (LDL) lipids is that LDL increases the concentrations of lipid peroxides, and that these peroxides inhibit the formation of prostacyclin (PGI_2) in vascular endothelium (6). A protective effect of selenium against hyperlipaemia-induced cardiosclerosis might therefore be exerted

through neutralisation of lipid peroxides by restoration of the capacity to form PGI_2. If this is true, subjects with high concentrations of LDL lipids would need higher serum concentrations of selenium for protection against the risks of increased peroxide formation.

In a recent investigation of the selenium status in diabetic children it was found that the serum level of this element was significantly higher in these children than in healthy controls (5). In patients with diabetes mellitus the lipid metabolism has been found to be defective and this defect seems to be related to the increased prevalence of cardiovascular disease found in this condition (11). Not only are the serum concentrations of lipoproteins abnormal in diabetic populations, but it has also been questioned whether the lipoproteins re qualitatively different from those in normal controls (8).

We have studied the relationships between the serum concentrations of selenium, lipoprotein lipids and proteins in healthy children and adolescents and in a group of diabetic children of similar ages with the aim of obtaining a basis for support or rejection of a hypothesized relationship indicating a protective mechanism against lipid peroxidation in young people with or without diabetes.

MATERIAL AND METHODS

The subjects of the present survey have been presented in several recent reports (2, 5). The study groups comprised 13 healthy children age 8-17 years and 27 children aged 5-18 years with Type I diabetes mellitus which had been diagnosed 2-15 years previously. The diabetic disease was being kept under relatively good control by means of standard clinical procedures currently in practice in Sweden. The children were being treated with two doses of monocomponent procine insulins. Their physical growth was normal compared with age- and sex-matched peers residing in the same geographical area (2). Fundoscopy was performed annually in all cases. None of the cihildren showed any signs of long-term diabetic complications.

Sera were taken in the fasting state at 07.45 - 08.30 before insulin and breakfast. Selenium was assayed by a neutron activation analysis method that has been developed for the determination of this element in biological samples, using the ^{75}Se nuclide as described in a previous publication (5). The serum lipid and apolipoprotein concentrations in these children (Table 1) and the analytical methods employed have been presented earlier (3, 4). The correlations between the individual serum lipid, lipoprotein and apolipoprotein concentrations and serum selenium were studied by means of a conventional computerized statistical programme (SAS on IBM 158-4341 at Uppsala University).

Table 1. Serum lipid and apolipoprotein (Apo) concentrations in diabetic children (D) and healthy controls (H).

	D	H
Chol, mmol/l	4.70±0.60	4.25±0.78
HDL Chol, mmol/l	1.55±0.30	1.29±0.27
TG, mmol/l	1.07±0.47	1.04±0.39
HDL TG, mmol/l	0.33±0.12	0.27±0.06
Apo A-I, AU	113±15	97±11
Apo A-II, AU	90±11	92±12
Apo B, AU	95±16	89±19
Apo C-II, g/mmol	2.7±0.8	2.5±0.8
Apo C-III, g/mmol	7.5±2.1	6.8±2.2

From Ewald et al (3). (TG in group D corrected. Misprint in 3.)

RESULTS

In the 13 healthy children serum selenium ranged between 5.5 and 8.2 (6.5±0.8) ug/100 ml, values which correspond to those found in a large group of healthy children from the same area (10). Serum selenium showed positive correlations with triglyceride and cholesterol concentrations in whole serum and very low density lipoproteins (VLDL) + LDL, but not with the high-density lipoprotein (HDL) fraction (Table 2). The highest correlation coefficient was found for non-HDL cholesterol (Fig. 1). No such correlation was observed for HDL cholesterol. Serum selenium also correlated positively both to serum apolipoprotein A II (Apo A II) and to serum Apo C III ($r=0.57$; $p<0.05$).

Table 2. Correlations between serum selenium concentration and the concentrations of cholesterol and triglycerides in whole serum and lipoprotein fractions in 13 healthy children.

	Whole serum	VLDL+LDL	HDL
Cholesterol	r=0.56	r=0.60	r=-0.04
	p<0.05	p<0.05	ns
Triglycerides	r=0.56	r=0.56	r =0.39
	p<0.05	p<0.05	ns

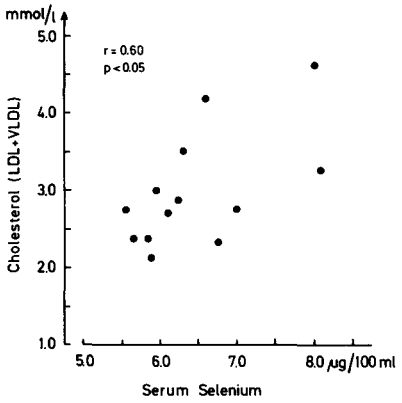

Figure 1. Relation between serum selenium and non-HDL cholesterol (VLDL+LDL cholesterol) in 13 healthy children and adolescents.

The mean serum selenium concentration was slightly but significantly higher (7.4±0.8 ug/100 ml) in the diabetic children than in the healthy controls (5). The diabetic children also had higher Apo AI and higher HDL cholesterol values in serum than the healthy controls (3, 4). The serum selenium concentration showed no significant correlation with the serum concentration of total cholesterol or total triglycerides or their HDL or non-HDL fractions, Apo AI, Apo B or Apo C in this group of diabetic patients. On the other hand, the serum selenium level was slightly but significantly correlated with the levels of Apo AII ($r=0.43$; $p<0.05$) and Apo CII ($r=0.42$; $p<0.05$). No significant correlation was found between the serum selenium concentration and the degree of diabetes control as reflected by haemoglobin A_1.

DISCUSSION

In vitro studies with use of ^{75}Se in humans have shown that selenium is bound to a greater degree with very low density lipoproteins and low-density lipoproteins than to high density lipoproteins (1). As VLDL is catabolized to LDL, selenium might be a natural constituent of human LDL and VLDL. In the late 1960s animal experiments using chicks established the roles of selenium and vitamin E along with glutathione peroxidase in preventing cell membrane damage by peroxides deriving from lipid metabolism (12, 13). It has been postulated that lipid peroxide formation is higher in the LDL fraction than in other lipoprotein fractions (6). Peroxidation of lipids, especially the long polyunsaturated fatty acids in cell membrane phospholipids, is potentially dangerous and might originate from free radical formation in biological tissues. Peroxidised products of arachidonic

acid are potent and selective inhibitors of prostacyclin formation (7). PGI_2 plays a role in the protection against intra-arterial thrombus formation and possibly also against myocardial infarction. If the danger of developing high levels of serum cholesterol and triglycerides, especially in the LDL fraction, is mediated through an increase in lipid peroxide formation, as suggested by Gryglewski and Szczeklik (6) the possibility of phophylaxis by means of radical scavengers such as selenium and vitamin E might be considered.

The data obtained in the present study of healthy children and adolescents indicate that there is a clear relationship between serum selenium and the lipoprotein fractions with a density of less than 1.063, i.e. VLDL and LDL. In healthy children the major fraction below this density is LDL. The correlation between serum selenium and non-HDL cholesterol (0.60), and the absolute lack of correlation with HDL cholesterol (r=0.04) suggest that selenium is more specifically associated with certain lipoproteins, and not merely related unspecifically with serum lipid fractions in general, supporting the hypothesis that the selenium level increases in response to elevated LDL concentrations in healthy young humans.

In diabetics, selenium was significantly correlated only with Apo AII and Apo CII. Apo CII activates lipoprotein lipase, which is involved in triglyceride mobilisation from lipoproteins (9). The slight correlation between serum selenium and Apo CII is difficult to interpret. It might be speculated that it reflects a role of selenium in triglyceride degradation. The marginal correlation with Apo AII might focus some further interest on triglyceride metabolism, as Apo AII in diabetic children is correlated to serum triglycerides but not to serum cholesterol, in contrast to the situation in healthy children (4). The avsence of a correlation between the increased serum selenium and serum cholesterol, the only lipid which showed an increased serum concentration in the group studied (3), is interesting and differs from the finding in healthy children.

In healthy mman selenium deficiency and abnormal lipoprotein patterns have been found to be associated with an increased risk of cardiovascular disease. The enhanced susceptibility of diabetics to acquire atherosclerotic cascular damage at an earlier stage and more frequently than the general population, and the possible relationship between this damage and lipoprotein metabolism, have been discussed extensively in numerous reports (3, 11). The data presented here do not support the possibility thaat the increased serum selenium in diabetic children is a response to peroxide formation if this formation parallels the LDL concentration. On the other hand, the findings are compatible with the view that diabetics have a less efficient response to peroxide formation. Another possibility is that peroxides are not associated with LDL lipids in diabetes. Direct measurements of free radical and lipid peroxide formation in diabetics with known serum selenium concentrations and erythrocyte glutathione peroxidase activity are required to elucidate this question.

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