

Reduced concentrations of selenium in mild Crohn's disease

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SUMMARY The concentrations of selenium, zinc, and copper were determined in whole blood, plasma, and leucocytes in 20 patients with relatively mild Crohn's disease, nine of whom were being treated with steroids, and compared with those of a control group. There was a significant decrease in the concentration of selenium in the leucocytes as well as in whole blood and plasma in the patients. Steroids seemed to affect only the concentrations of zinc and copper in plasma. The concentrations of copper and zinc in whole blood, plasma, and leucocytes in patients not taking steroids were not significantly different from those of the control group. The observations suggest that those patients with an apparently satisfactory whole body concentration of copper and zinc may still be at risk of a decrease in the body content of selenium.

The essential role of zinc and copper as components of metalloenzymes and metalloproteins has been established.^{1,2} Although the biological function of selenium in man is less well defined, it is an essential constituent of the enzyme glutathione peroxidase (EC 1.11.1.9), which protects membrane structures by detoxifying oxygen species.³ Copper, zinc, and selenium are absorbed from the small intestine,^{1,4} and any inflammatory condition or malabsorptive state may lead to defective uptake. Studies using animal models indicate that absorption of the trace elements is facilitated by specific low molecular weight ligands in the intestinal lumen and mucosa as well as in pancreatic secretions.^{5,6} The presence of excess lipid and other malabsorbed products may impair absorption of trace elements by the formation of insoluble complexes.⁷

Of the methods currently used to assess body trace element state, none is ideal. Plasma concentrations of copper and zinc in particular are subject to non-specific effects such as infections, trauma, and administered steroids. No single technique for assessing selenium content has proved entirely satisfactory. Selenium concentrations in blood seem to correlate well with the selenium content of skeletal muscle in rats fed a constant amount of selenium, although plasma selenium concentrations do not always represent the state of the muscle pool.⁸ Trace element concentrations in leucocytes may be the most satisfac-

tory method for semiroutine use to assess body trace element state. Reduced concentrations of zinc in leucocyte have been reported in healthy volunteers who received a zinc deficient diet for several weeks,⁹ and reduced zinc concentrations in leucocytes have been reported in various disorders in which zinc deficiency may be a complication.^{10,11}

The purpose of the study was to assess body trace element state of selenium, zinc, and copper in patients with Crohn's disease by determining concentrations in leucocytes; concentrations were also determined in plasma and whole blood.

Patients and methods

Twenty ambulatory patients with Crohn's disease (16 women and four men, aged 21–54 (mean 40.2) years) were studied. Diagnosis had been established by radiographic and clinical criteria. Ten patients had disease of the small bowel alone and 10 of both small and large bowel. None of them had been in hospital in the previous 12 months, although two patients had undergone previous partial resections of the bowel. Chronic inflammatory bowel disease was the only disease identified. Nine patients had quiescent disease and of these four were receiving prednisolone. Eleven patients complained of chronic diarrhoea and these included five who were receiving prednisolone. None of the female patients was taking contraceptives. Normal serum B12 and red cell folate concentrations had been reported on all patients within three months

Table 1 Details of analyses

| Analysis | Method | Interbatch precision (%) |
|--|--|--------------------------|
| Plasma zinc Plasma copper Whole blood zinc Whole blood copper Leucocyte zinc | Flame atomisation and atomic absorption spectrophotometry ^{13,15} | 3.1 |
| | | 3.9 |
| | | 2.1 |
| | | 4.1 |
| | | 3.8 |
| Leucocyte copper | Electrothermal atomisation and atomic absorption spectrophotometry ¹³ | 4.6 |
| Plasma selenium Whole blood selenium Leucocyte selenium | Hydride generation and atomic absorption spectrophotometry ¹⁶ | 4.9 |
| | | 4.9 |
| | | 5.9 |
| Albumin | Colorimetry | 3.1 |

of the start of the study. The mean body mass index¹² was 21.5 (15.5–30.1). By these criteria six of the patients were below their normal weight and of these four suffered from diarrhoea. Frequency of bowel movements in these patients varied between two and six times a day.

Venous blood was collected between 09.00 and 11.00 hours. Leucocytes were separated using a dextran sedimentation technique.¹³ Table 1 gives details of the methods and interbatch precision of analysis.

The study had the approval of the joint ethical subcommittee of the faculty of medicine of the University of Southampton and Southampton and South West Hampshire Health Authority.

Statistical analysis

The patient data were matched for age, sex, and smoking habits against control data obtained from previous work carried out in this unit.¹⁵ Each patient was matched with two control subjects. The age range for the 40 adult healthy controls was 21–59 (mean 40.0) years.

All measurements relating to copper and selenium, and zinc measurements in plasma and whole blood, were more or less normally distributed. Those for zinc in leucocytes were skewed and results were subjected to logarithmic transformation to achieve approximate normality.

The Mann-Whitney U test was used to compare the leucocyte zinc concentrations and a paired *t* test for the normally distributed results. Pearson's product-moment correlation coefficient (*r*) was calculated to assess the association between variables. Data are given as mean ± 1 standard deviation unless otherwise stated.

Results

To investigate the effect of steroids on zinc, copper,

and selenium concentrations, patients taking steroids (*n* = 9) were matched for sex, smoking habit, and presence or absence of diarrhoea with those patients not taking steroids. Comparison of the data relating to these two groups showed significantly lower (*p* < 0.05) concentrations of plasma zinc and significantly higher (*p* < 0.05) concentrations of plasma copper in patients taking steroids. There were no significant differences between these two groups for the concentrations of zinc or copper in leucocytes or whole blood.

The copper and zinc concentrations for the patients not taking steroids (*n* = 11) and the matched controls

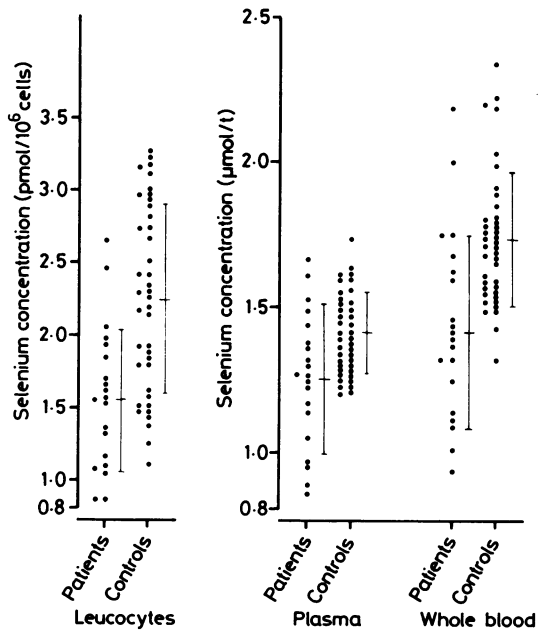


Figure Scattergram of selenium concentrations in leucocytes, plasma, and whole blood in patients with Crohn's disease and in controls. Bars indicate mean ISD.

Table 2 Concentrations of zinc and copper in patients not taking steroids and matched controls

| Analysis | Patients not taking steroids (n = 11) (mean \bar{x}_1) | Matched controls (n = 22) (mean \bar{x}_2) | Ratio of means (\bar{x}_1/\bar{x}_2) (a) or mean of individual patient-control differences (b) | 95% confidence intervals for ratio of means (\bar{x}_1/\bar{x}_2) (a) or mean of individual patient-control differences (b) |
|---|--|--|--|---|
| Leucocyte zinc pmol/10 ⁶ cells | 106.5 (90-127)* | 111.0 (96-121)* | 0.96 (a) | 0.89 to 1.04 (a) |
| Plasma zinc μ mol/l | 12.7 (1.8) | 12.9 (1.7) | -0.25 (b) | -1.31 to 0.81 (b) |
| Whole blood zinc μ mol/l | 89.2 (11.6) | 87.9 (10.2) | 1.27 (b) | -7.86 to 10.40 (b) |
| Leucocyte copper pmol/10 ⁶ cells | 10.0 (4.3) | 9.8 (4.2) | 0.15 (b) | -3.37 to 3.67 (b) |
| Plasma copper μ mol/l | 17.3 (3.3) | 16.3 (2.6) | 0.92 (b) | -1.55 to 3.39 (b) |
| Whole blood copper μ mol/l | 14.2 (1.4) | 14.0 (1.7) | 0.18 (b) | -1.08 to 1.44 (b) |

*Geometric mean as results are skewed (interquartile distance).

(n = 22) are shown in table 2. There was no significant difference for the concentrations of zinc or copper in plasma, whole blood, or leucocytes between these two groups. A significant decrease in the concentration of selenium in leucocytes (p < 0.001), plasma, and whole blood (p < 0.01), however, was found in the total number of patients with Crohn's disease (n = 20) when compared with the control subjects (n = 40) (figure).

There were no significant correlations (p > 0.05) between the presence of diarrhoea in the patients and selenium concentrations in leucocytes, plasma or whole blood. Similarly, no significant correlations were shown between the presence of diarrhoea in the patients with Crohn's disease not taking steroids, and zinc or copper concentrations in leucocytes, plasma, or whole blood.

In patients and controls a significant correlation was shown between selenium in leucocytes and plasma (p < 0.001, r = 0.73; p < 0.05, r = 0.51, respectively) and selenium in leucocytes and whole blood (p < 0.001, r = 0.73; p < 0.05, r = 0.46, respectively). No similar correlations was noted for copper and zinc.

Plasma albumin concentrations (mean SD) were similar in patients (39 (4) g/l) and matched controls (40 (4) g/l), and there was no correlation between plasma zinc and albumin or plasma selenium and albumin in either of the groups.

Discussion

Reduced concentrations of selenium were observed in whole blood, plasma, and leucocytes in the patients whether or not they were receiving steroids. Jacobson *et al* reported low plasma and erythrocyte selenium concentrations in Crohn's disease,¹⁷ although these patients were inpatients with severe disease about to undergo preoperative total parenteral nutrition. As already discussed, the patients in this study were outpatients with reasonably quiescent disease, and this may well have been reflected by the lack of any clinically important findings for copper and zinc, apart

from the apparent effect of steroids. This agrees with previous studies where a significant decrease in plasma zinc has been described in patients with severe Crohn's disease¹⁸⁻²⁰ but not in outpatients with clinically quiescent disease.²¹

Trace element deficiency may be caused by reduced intake, decreased absorption, or increased loss. Although deficiency of copper and zinc seems most likely to occur when extensive disease is present, selenium seems to be reduced in patients with relatively stable disease. In previous work undertaken by this unit reduced selenium concentrations were found in a group of patients with coeliac disease who were considered to be clinically well,²² but no significant decrease was noted in the concentrations of copper or zinc (Hinks LJ, *et al*, Abstract presented to XII International Congress on Nutrition, 1985). A more recent study has shown similar findings in patients with eczema and psoriasis.²³ The clinical importance of lowered selenium concentrations in these patients requires further investigation. Although the effect of experimental selenium deficiency in animals has been reviewed,²⁴ the role of selenium in human metabolism is less well understood. Epidemiological studies have suggested that a low selenium intake may increase the risk of malignant complications,²⁵ and an inverse relation between selenium and mortality due to heart disease has been shown.²⁶ Although excessive dietary supplementation of selenium can be toxic,²⁷ studies are needed to determine whether administration of selenium supplement would be beneficial to patients who seem to have a low body content of selenium.

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