Alimentary tract and pancreas

Concentration of selenium in plasma and erythrocytes during total parenteral nutrition in Crohn's disease

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SUMMARY Plasma- and erythrocyte-selenium concentrations were determined in five consecutive patients with Crohn's disease given preoperative total parenteral nutrition – nil *per os* – for a mean period of 34 days per patient. No blood components were administered during the total parenteral nutrition. Before the total parenteral nutrition the plasma-selenium level and, to a less extent, the erythrocyte-selenium levels were below the reference values. After three weeks of total parenteral nutrition both concentrations had fallen. There were, however, clinical and biochemical signs of improvement during the total parenteral nutrition, as indicated by an increase in body weight, P-albumin and P-transferrin. In one female patient given 39 days of preoperative total parenteral nutrition containing 0.06 μmol (5 μg) selenium per 24 h the decreasing levels of plasma-selenium and erythrocyte-selenium were both correlated to the duration of the total parenteral nutrition ($r=0.87$ and 0.96 , respectively). The results suggest that total parenteral nutrition patients may be at risk for selenium deficiency, and that a supplementary administration of selenium *via* total parenteral nutrition may be required.

Total parenteral nutrition has become a valuable aid in the care of patients with Crohn's disease.^{1,2} As many patients with Crohn's disease show multiple and sometimes severe nutritional deficiencies,³ the total parenteral nutrition solutions should not lack any essential nutrient that might aggravate an existing deficiency.

Selenium deficiency has been observed in adults receiving parenteral nutrition,^{4,5} and may cause fatal cardiomyopathy during such a treatment.⁶ As we have found very low concentrations of selenium in whole blood in patients with Crohn's disease,⁷ the present study of both plasma and erythrocyte concentrations of selenium in such patients receiving total parenteral nutrition, including commercially available solutions, was performed with an improved method for selenium analysis.

Methods

PATIENTS

The series for this study consisted of five consecutive patients with Crohn's disease (one man and four

women), who were given total parenteral nutrition (nil *per os*), without blood transfusion or blood components, for more than three weeks. The total parenteral nutrition was administered preoperatively on clinical grounds. The diagnosis of Crohn's disease was based on the findings at clinical, radiographic and histologic examinations.^{8,9} Bowel resection was performed on total parenteral nutrition days 23–56. The period of the study consisted only of the preoperative days of total parenteral nutrition (mean, 34 days per patient; range, 22–55 days per patient).

The clinical data relating to the patients are presented in Table 1. Four of the patients had had

Table 1 Clinical data for five patients with Crohn's disease on introduction of total parenteral nutrition (TPN)

	Mean	SD
Age (yr)	39	13
Height (m)	1.67	0.06
Body weight (kg)	48	6
Body mass index* (units)	17.1	1.5
Crohn's disease activity index (units) ³³	329	104

* Weight/(height)²

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Received for publication 23 March 1984

an operation. At the time the total parenteral nutrition was introduced one patient had jejuno-colitis (after several resections of the small intestine and the ascending colon), two had ileitis (after ileocecal resections), one ileocolitis and one colitis (after resection of the sigmoid colon). Two patients were given prednisolone; the initial doses of 12.5 and 40 mg/24 h were gradually reduced during the preoperative days of total parenteral nutrition.

INFUSION SOLUTIONS AND PROCEDURE

The infusion solutions included amino acids (Vamin with glucose, KabiVitrum AB, Stockholm, Sweden),¹⁰ carbohydrates, fat emulsion (Intralipid 10%, KabiVitrum),¹¹ electrolytes, trace elements (Addamel, KabiVitrum) and vitamins (Soluvit and Vitalipid Adult, KabiVitrum).¹² The total parenteral nutrition regimens provided 9.8–13.1 MJ (2350–3100 kcal) of energy per 24 h (8.8–11.5 non-protein MJ/24 h), including 56 g fat, 287.5–437.5 g glucose, 112.5 g fructose, 9.4–14.1 g nitrogen, 11.25 g glycerol and 4.5 g sorbitol.

The intravenous infusions were given for about 14 hours daily (08.00–22.00 h) by gravity drip through a central venous catheter.¹³ In two patients 0.5 l of Intralipid 10%, including the vitamins, was given from 08.00 to 10.00 h, followed, until 22.00 h, by a mixture of the other infusion components, delivered from the pharmacy in a 3-litre plastic bag (Travenol, Thetford, Norfolk, England). In the other three patients the fat emulsion (given from 08.00 to 14.00 h) and the mixture of the other infusion components (given from 08.00 to 22.00 h) were mixed when passing through the central venous catheter. To reduce the risk of central venous catheter-related thrombosis all the patients were given heparin intravenously, 5000 IU/6 h.¹⁴

ANALYTICAL METHODS

Venous blood samples were drawn after an overnight fast (12–14 h) before total parenteral nutrition

was introduced, and between 07.00 and 08.00 h – before the daily infusion was started – at intervals during total parenteral nutrition. The concentrations of albumin, haptoglobin, orosomucoid, and transferrin in the blood plasma (P-) were determined by the conventional methods used at Huddinge Hospital, as also were the haemoglobin concentration in blood.

The selenium concentration in the samples was determined by neutron activation analysis.¹⁵ Approximately 0.5 g of plasma and 0.5 g of erythrocytes were freeze-dried in quartz ampoules under conditions designed to avoid contamination. The quartz ampoules were sealed in an oxygen-hydrogen flame and then irradiated in the Norwegian nuclear reactor JEEP II at Kjeller for one week at a flux of $2 \times 10^{13} \text{ n cm}^{-2} \text{ s}^{-1}$. The samples were dissolved in acids. Selenium was precipitated and counted as described elsewhere.¹⁵

The method of statistical analysis of the results was Student's *t* test for paired and unpaired data. Differences were considered to be significant at the level $p < 0.05$. Regression lines were calculated by the method of least squares. All the results are reported as the mean $\pm$ SD.

Results

During total parenteral nutrition all five patients displayed clinical remission – as judged from their well-being, relief of abdominal pain and abatement of diarrhoea. Throughout the period of preoperative total parenteral nutrition the body weight increased significantly from 48 ± 6 to 51 ± 7 kg.

The results of the biochemical analyses are summarised in Table 2. Throughout the period of preoperative total parenteral nutrition the P-albumin concentration increased from 30 ± 3 to 38 ± 4 g/l; the numerical decrease in P-orosomucoid from 1.7 ± 0.5 to 1.3 ± 0.4 g/l was not significant ($p = 0.08$).

The results of the analyses of the selenium

Table 2 Blood (B-) concentration of haemoglobin and plasma (P-) concentrations of three proteins measured during TPN in the five patients with Crohn's disease

Component	During TPN												Reference range
	Before IPN			Days 7–10			Day 15			Days 21–23			
	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	
B-haemoglobin (g/l)	104	9	5	104	12	5	109	5	5	116	15	4	115–165
P-albumin (g/l)	30	3	5	33	3	5	35*	3	5	36*	5	4	38–55
P-transferrin (g/l)	1.7	0.5	3	2.2*	0.7	3	2.5	0.7	3	2.7	1.3	3	2.1–3.6
P-haptoglobin (g/l)	2.9	1.0	5	2.6*	1.0	5	3.0	1.7	5	2.1*	1.2	4	0.4–2.0

* Significant difference from the value before TPN ($p < 0.05$).

concentrations in plasma and erythrocytes are summarised in Table 3. After three weeks of total parenteral nutrition the plasma-selenium and erythrocyte-selenium concentrations had decreased, even though both were below the reference values when total parenteral nutrition was introduced. In one female patient, who had the highest initial concentration of erythrocyte-selenium of all the patients, the concentrations of plasma-selenium and erythrocyte-selenium were both correlated to the duration of the preoperative total parenteral nutrition ($r=0.87$ and $r=0.96$, respectively) (Figure). Four analyses of the total parenteral nutrition solutions showed that she had received about $5\text{ }\mu\text{g}$ ($0.06\text{ }\mu\text{mol}$) of selenium per 24 hours, $1\text{ }\mu\text{g}$ of which was present in the 0.5 l of Intralipid 10%, including the vitamins.

Discussion

Depletion of trace elements, including chromium, copper, molybdenum, selenium and zinc, has been observed in patients receiving their total nutritional needs from intravenous solutions.^{4 16-19} One trace element that is not added to total parenteral nutrition solutions in Sweden and many other parts of the world is selenium; this is an essential component of the cytosol enzyme, glutathione peroxidase (GSH-Px), which is concerned in the metabolism of hydrogen peroxide.²⁰⁻²²

The nutritional status in respect of selenium can be determined by measuring the selenium concentration and the GSH-Px activity in the blood.²⁰ The blood selenium concentration and the GSH-Px activity have been found to be positively correlated in animals and healthy New Zealand^{23 24} and American²⁵ populations.

A positive correlation between erythrocyte GSH-Px activity and plasma selenium concentration has been found in patients given parenteral nutrition but

Figure In one female patient given preoperative total parenteral nutrition for 39 days the concentrations of selenium in erythrocytes (O, y_1) and in plasma (●, y_2), were correlated to the duration of the total parenteral nutrition (x), as described by the regression equations: $y_1=102-0.722x$ and $y_2=54.4-0.438x$, respectively. Corresponding correlation coefficients (r) were 0.96 and 0.87.

not between erythrocyte selenium concentration and GSH-Px activity.⁵ This may be because only a small part of the erythrocyte selenium is bound to GSH-Px, and that these two pools of erythrocyte selenium may change at different rates.²⁶

In the Crohn's disease patients of the present study there was a decrease in the plasma and erythrocyte concentrations of selenium during total parenteral nutrition, including commercially available infusion solutions but no supplementary selenium. This decrease is remarkable in view of the fact that the concentrations of selenium in the plasma and the erythrocytes point to selenium deficiency already at the time that total parenteral nutrition was introduced. The clinical significance of this degree of low blood selenium concentrations is,

Table 3 Plasma (P-) and erythrocyte (E-) concentrations of selenium measured during TPN in the five patients with Crohn's disease

Component	During TPN																		Reference value			
	Before TPN			Day 7-10			Day 15			Days 21-22			Days 27-29			Day 36		Day 50				
	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	n	Mean	n	Mean	SD	n
P-selenium (ng/g)	45	15	5	39*	17	4	45	19	3	37*	12	5	39*	16	3	39	2	43	1	81†	14	50
E-selenium (ng/g)	78	17	5	70	22	4	72	15	3	65*	12	5	66	17	3	71	2	56	1	100*	19	50

* Significant difference from the value before TPN ($p<0.05$).
† Significant difference from the value before TPN ($p<0.001$).

however, unknown.

Though the total parenteral nutrition regimen obviously aggravated the deficiency of selenium, there was clinical and biochemical evidence of a nutritional improvement during the total parenteral nutrition, as indicated by the increase in body weight, P-albumin and P-transferrin. The possible concomitant abatement of the inflammation of the bowel, as reflected in the changes in the biochemical variables studied, was less convincing, as there was a decrease only in P-haptoglobin, and no significant change in P-orosomucoid.

The female patient represented in the Figure had an erythrocyte volume fraction of about 35% throughout the 39 days of preoperative total parenteral nutrition. If a blood volume of 5 litres is assumed, the 24-hour loss of selenium in this patient during the total parenteral nutrition would have been 16 nmol (1.3 µg) from the erythrocytes and 18 nmol (1.4 µg) from the blood plasma, or 34 nmol (2.7 µg) from the whole blood volume. In Crohn's disease patients on a similar selenium-poor total parenteral nutrition regimen to that of the present study the 24-hour urinary selenium excretion was 43–57 nmol (3–5 µg);¹³ this is of the same magnitude as the calculated loss from the blood compartment of the female patient in question.

Neither a low dietary selenium intake nor a low blood selenium concentration has been found to be related to any specific pathologic condition in man.⁵ A low selenium concentration in serum, however, has been associated with an increased risk of gastrointestinal and prostatic cancer.²⁷ New Zealanders who consume less than 50 µg of dietary selenium a day were not observed to have any specific disease,²⁴ whereas Chinese children and women of child-bearing age living in a specific region and consuming less than 30 µg selenium/day frequently developed a cardiomyopathy called Keshan's disease.^{28,29} This disease can be prevented, though not cured, by dietary supplementation of sodium selenite.

The total parenteral nutrition solutions and additives used in this study provided only about 5 µg of selenium per 24 hours. In total parenteral nutrition solutions used in USA, however, up to 300 µg of selenium per litre has been found as a contaminant.^{30,31}

Selenium supplementation in patients on long term parenteral nutrition has received little attention, and no intravenous selenium preparation is commercially available in Sweden.

Because of the inter-subject variability and the potential toxicity of selenium³² it has been recommended that an assessment of the selenium status should be performed before adding the element to

the infusion solution, and repeated at intervals during the administration of supplementary selenium.⁵

In view of the fact that, despite initially subnormal values, our patients showed a decrease in the plasma and erythrocyte selenium concentrations over so short a period of total parenteral nutrition as three weeks, and as our infusion solutions are poor in selenium, it would seem important to administer the element to selenium-deficient total parenteral nutrition patients.

References

- 1 Milewski PH, Irving MH. Parenteral nutrition in Crohn's disease. *Dis Colon Rectum* 1980; **23**: 395–400.
- 2 Lehr L, Schober O, Hundeshagen H, Pichlmayr R. Total body potassium depletion and the need for preoperative nutritional support in Crohn's disease. *Ann Surg* 1982; **196**: 709–14.
- 3 Driscoll Jr RH, Rosenberg IH. Total parenteral nutrition in inflammatory bowel disease. *Med Clin N Am* 1978; **62**: 185–201.
- 4 van Rij AM, Thomson CD, McKenzie JM, Robinson MF. Selenium deficiency in total parenteral nutrition. *Am J Clin Nutr* 1979; **32**: 2076–85.
- 5 Lane HW, Barroso AO, Englert D, Dudrick SJ, MacFadyen Jr BS. Selenium status of seven chronic intravenous hyperalimentation patients. *J Parent Ent Nutr* 1982; **6**: 426–31.
- 6 Fleming CR, Lie JT, McCall JT, O'Brien JF, Baillie EE, Thistle JL. Selenium deficiency and fatal cardiomyopathy in a patient on home parenteral nutrition. *Gastroenterology* 1982; **83**: 689–93.
- 7 Jacobson S, Plantin LO. Spårelementkoncentrationer i helblod vid långvarig total parenteral nutrition. *Svensk Kirurgi* 1979; **37**: 168–9.
- 8 Price AB, Morson BC. Inflammatory bowel disease. The surgical pathology of Crohn's disease and ulcerative colitis. *Hum Pathol* 1975; **6**: 7–29.
- 9 Goldberg HI, Caruthers Jr SB, Nelson JA, Singleton JW. Radiographic findings of the national cooperative Crohn's disease study. *Gastroenterology* 1979; **77**: 925–37.
- 10 Jacobson S. Serum concentrations and urinary excretion of amino acids during total parenteral nutrition after abdominal surgery. *J Parent Ent Nutr* 1982; **6**: 204–13.
- 11 Grotte G, Jacobson S, Wretling A. Lipid emulsions and technique of peripheral administration in parenteral nutrition. In: Fischer JE, ed. *Total parenteral nutrition*. Boston: Little, Brown & Co, 1976: 335–62.
- 12 Jacobson S, Wester PO. Balance study of twenty trace elements during total parenteral nutrition in man. *Br J Nutr* 1977; **37**: 107–26.

- 13 Jacobson S, Plantin LO, Carlmark B. Urinary excretion and blood concentrations of trace elements and electrolytes during total parenteral nutrition in Crohn's disease. *Dig Dis Sci* 1984; **29**: 606-13.
- 14 Brismar B, Hårdstedt C, Jacobson S, Kager L, Malmberg AS. Reduction of catheter-associated thrombosis in parenteral nutrition by intravenous heparin therapy. *Arch Surg* 1982; **117**: 1196-9.
- 15 Plantin LO, Meurling S, Strandvik B. Selenium levels in Swedish children determined with a simple neutron activation analysis method. In *Mineral elements '80*. Proceedings, part 2, of a Nordic symposium on soil-plant-animal-man interrelationships and implications to human health. Helsinki: Mineral elements '80, Box 330, 00101 Helsinki 10, 1981: 453-7.
- 16 Jeejeebhoy KN, Langer B, Tsallas G, Chu RC, Kuksis A, Anderson GH. Total parenteral nutrition at home: studies in patients surviving 4 months to 5 years. *Gastroenterology* 1976; **71**: 943-53.
- 17 Solomons NW, Layden TJ, Rosenberg IH, Vo-Khactu K, Sandstead HH. Plasma trace metals during total parenteral alimentation. *Gastroenterology* 1976; **70**: 1022-5.
- 18 Jeejeebhoy KN, Chu RC, Marliss EB, Greenberg GR, Bruce-Robertson A. Chromium deficiency, glucose intolerance, and neuropathy reversed by chromium supplementation, in a patient receiving long-term total parenteral nutrition. *Am J Clin Nutr* 1977; **30**: 531-8.
- 19 Abumrad NN, Schneider AJ, Steel D, Rogers LS. Amino acid intolerance during prolonged total parenteral nutrition reversed by molybdate therapy. *Am J Clin Nutr* 1981; **34**: 2551-9.
- 20 Rotruck JT, Pope AI, Ganther HE, Swanson AB, Hafeman DG, Hoekstra WG. Selenium: biochemical role as a component of glutathione peroxidase. *Science* 1973; **179**: 588-90.
- 21 Forstrom JW, Zakowski JJ, Tappel AL. Identification of the catalytic site of rat liver glutathione peroxidase as selenocysteine. *Biochem* 1978; **17**: 2639-44.
- 22 Stadtman TC. Selenium-dependent enzymes. *Ann Rev Biochem* 1980; **49**: 93-110.
- 23 Thomson CD, Rea HM, Doesburg VM, Robinson MF. Selenium concentrations and glutathione peroxidase activities in whole blood of New Zealand residents. *Br J Nutr* 1977; **37**: 457-60.
- 24 Thomson CD, Robinson MF. Selenium in human health and disease with emphasis on those aspects peculiar to New Zealand. *Am J Clin Nutr* 1980; **33**: 303-23.
- 25 Lane HW, Dudrick S, Warren DC. Blood selenium levels and glutathione-peroxidase activities in university and chronic intravenous hyperalimentation subjects. *Proc Soc Exptl Biol Med* 1981; **167**: 383-90.
- 26 Behne D, Wolters W. Selenium content and glutathione peroxidase activity in the plasma and erythrocytes of non-pregnant and pregnant women. *J Clin Chem Clin Biochem* 1979; **17**: 133-5.
- 27 Willett WC, Morris JS, Pressel S, et al. Prediagnostic serum selenium and risk of cancer. *Lancet* 1983; **2**: 130-4.
- 28 Keshan Disease Research Group of the Chinese Academy of Medical Sciences. Observations on effect of sodium selenite in prevention of Keshan disease. *Chin Med J* 1979; **92**: 471-6.
- 29 Keshan Disease Research Group of the Chinese Academy of Medical Sciences. Epidemiologic studies on the etiologic relationship of selenium and Keshan disease. *Chin Med J* 1979; **92**: 477-82.
- 30 Smith JL, Goos SM. Selenium nutriture in total parenteral nutrition: intake levels. *J Parent Ent Nutr* 1980; **4**: 23-6.
- 31 Huston RK, Benda GI, Carlson CV, Shearer TR, Reynolds JW, Neerhout RC. Selenium and vitamin E sufficiency in premature infants requiring total parenteral nutrition. *J Parent Ent Nutr* 1982; **6**: 507-10.
- 32 Burk RF. Selenium in man. In: Prasad AS, ed. *Trace elements in human health and disease*. Vol 2. New York: Academic Press, 1976: 105-33.
- 33 Best WR, Beckett JM, Singleton JW, Kern Jr F. Development of a Crohn's disease activity index. National cooperative Crohn's disease study. *Gastroenterology* 1976; **70**: 439-44.