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...
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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 ileocecval 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),
carbohydrates, fat emulsion (Intralipid 10%, KabiVitrum),
electrolytes, trace elements (Addamel, KabiVitrum) and vitamins (Soluvit and Vitalipid Adult, KabiVitrum). The total
parenteral nutrition regimen 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
112.5 g glucose, 9.4–14.1 g
11.25 g gycerol 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. 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.

ANALYTICAL METHODS
Venous blood samples were drawn after an over-
night 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 concentra-
tions of albumin, haptoglobin, orosomucoid, and
transferrin in the blood plasma (P-) were deter-
mined 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. Approximately 0.5 g of plasma and 0.5 g of
erthrocytes 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 x 1013 n cm−2 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±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

<table>
<thead>
<tr>
<th>Component</th>
<th>Before IP</th>
<th>Days 7–10</th>
<th>Day 15</th>
<th>Days 21–23</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>n</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>B-haemoglobin (g/l)</td>
<td>104</td>
<td>9</td>
<td>5</td>
<td>104</td>
<td>12</td>
</tr>
<tr>
<td>P-albumin (g/l)</td>
<td>30</td>
<td>3</td>
<td>5</td>
<td>33</td>
<td>3</td>
</tr>
<tr>
<td>P-transferrin (g/l)</td>
<td>1.7</td>
<td>0.5</td>
<td>3</td>
<td>2.2*</td>
<td>0.7</td>
</tr>
<tr>
<td>P-haptoglobin (g/l)</td>
<td>2.9</td>
<td>1.0</td>
<td>5</td>
<td>2.6*</td>
<td>1.0</td>
</tr>
</tbody>
</table>

* 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 μg (0.06 μmol) of selenium per 24 hours, 1 μg 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. 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.

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

A positive correlation between erythrocyte GSH-Px activity and plasma selenium concentration has been found in patients given parenteral nutrition but not between erythrocyte selenium concentration and GSH-Px activity. 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.

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

<table>
<thead>
<tr>
<th>Component</th>
<th>Before TPN</th>
<th>Day 7–10</th>
<th>Day 15</th>
<th>Days 21–22</th>
<th>Days 27–29</th>
<th>Days 36</th>
<th>Day 50</th>
<th>Reference value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>n</td>
<td>Mean</td>
<td>SD</td>
<td>n</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>P-selenium (ng/g)</td>
<td>45±15</td>
<td>5</td>
<td>39*</td>
<td>17</td>
<td>4</td>
<td>45</td>
<td>19</td>
<td>3</td>
</tr>
<tr>
<td>E-selenium (ng/g)</td>
<td>78</td>
<td>17</td>
<td>5</td>
<td>70</td>
<td>22</td>
<td>4</td>
<td>72</td>
<td>15</td>
</tr>
</tbody>
</table>

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


Concentration of selenium in plasma and erythrocytes during total parenteral nutrition in Crohn's disease.
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doi: 10.1136/gut.26.1.50

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