Essential fatty acid deficiency in patients receiving home parenteral nutrition\(^1,2\)

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**ABSTRACT** Home parenteral nutrition (HPN), initiated in patients with severe malabsorption or decreased oral intake, may exhaust stores of essential fatty acids and cause clinical manifestations, mainly dermatitis. Plasma fatty acid profiles were measured by gas-liquid chromatography in 37 healthy control subjects and 56 patients receiving HPN. The concentration (\(\%\) by wt of total fatty acids) of 18:2\(\_n\_6\) was 22.8\% and 11.4\% \((P < 0.001)\), whereas 18:3\(\_n\_3\) was 0.2\% and 0.1\% \((P < 0.01)\) in control subjects and patients, respectively. Reduced small bowel length was associated with aggravated biochemical signs of essential fatty acid deficiency (EFAD). The effect of parenteral lipid on plasma phospholipids was evaluated in subgroups of patients. In patients with > 200 cm of remaining small intestine, those receiving parenteral lipids had only minor changes in the fatty acids of plasma phospholipids compared with patients not receiving parenteral lipids. In patients with < 100 cm of remaining small intestine, those receiving parenteral lipids had increased concentrations of total n–6 fatty acids; however, these did not reach the concentrations in control subjects. Twenty-five of the 56 patients receiving HPN reported skin problems. No differences were seen in n–3 fatty acids. Twenty-five of the 56 patients receiving HPN reported skin problems. No differences were found in plasma phospholipid fatty acids, Holman index, or plasma in the total cohort of 56 patients receiving HPN in our institution. The relation between remaining small intestinal length, supply of parenteral lipid and EFAs, and biochemical evidence of EFAD was investigated. In addition, the association between biochemical and clinical manifestations of EFAD was evaluated.

**KEY WORDS** Essential fatty acid deficiency, plasma phospholipids, linoleic acid, eicosatrienoic acid, Holman index, home parenteral nutrition, short bowel syndrome, humans

**INTRODUCTION** Severe malabsorption of the essential fatty acids [linoleic (18:2\_n\_6) and linolenic acid (18:3\_n\_3)] (1), low dietary intake (2), and increased physical requirements (3) may lead to essential fatty acid deficiency (EFAD). Sinclair (4) was the first to emphasize the possible importance of abnormalities of essential fatty acid (EFA) intake or metabolism in human disease. He argued that not only skin diseases but many of the chronic diseases of modern humans (atheromatous cardiovascular diseases, complications of diabetes, chronic inflammatory conditions, osteoporosis, renal stones, and disorders of development and function of the visual system and the brain) might be related to a chronic relative deficiency of EFAs or to a defect in EFA metabolism (5).

Long-term home parenteral nutrition (HPN) is initiated in patients with chronic intestinal failure, reduced intestinal absorptive surface, severe malabsorption, and short bowel. In a smaller proportion of patients, such as patients with intestinal motility disorders and pseudoobstruction, HPN is required because of insufficient food intake. Patients receiving HPN thereby differ in their fat and energy intake and in their ability to absorb fat, and may exhaust their stores of EFAs. Even patients not receiving HPN who have a certain degree fat malabsorption of (> 20 g/d) may develop biochemical signs of EFAD (6).

Patients receiving total parenteral nutrition (TPN), in association with diseases that force oral intake of food to be discontinued or dramatically reduced, develop biochemical signs of EFAD within days to weeks (7–9) and have been reported to be at risk of clinical manifestations, mainly dermatitis (10, 11). Hepatic steatosis (12), hematologic disturbances (13), and diminished immune system status (14) have also been related to EFAD. Clinical signs of EFAD, however, may not appear for weeks or months, and impede clinical interpretation of biochemical changes in blood concentrations of EFAs. Little is known of the EFA status of patients receiving HPN (15, 16), and guidelines on the amount and necessity of intravenous lipid supplementation in HPN patients are sparse (17).

This study evaluated essential and nonessential fatty acids in plasma in the total cohort of 56 patients receiving HPN in our institution. The relation between remaining small intestinal length, supply of parenteral lipid and EFAs, and biochemical evidence of EFAD was investigated. In addition, the association between biochemical and clinical manifestations of EFAD was evaluated.
ESSENTIAL FATTY ACIDS AND HPN

SUBJECTS AND METHODS

Patients

Fifty-eight patients receiving HPN who were being treated at the Department of Gastroenterology, Rigshospitalet, Copenhagen, in June 1995, were invited to participate. Two patients declined. Of the remaining 56 patients, 40 were women and 16 were men. Mean age was 49.8 ± 15.7 y (range: 16.8–76.2 y). All patients were clinically stable and received, 3–7 times a week, some form of nocturnal cyclic nutrition or fluids. The mean duration of HPN was 5.2 y (range: 0.2–25.5 y). The study was approved by the Ethical Committee for Medical Research in Copenhagen and conducted according to the Helsinki II Declaration.

Thirty patients had Crohn disease (20 women and 10 men; mean age: 44.6 ± 12.9 y) and 5 had intestinal resections because of ileus or supervening complications of abdominal surgery (4 women and 1 man; mean age: 49.5 ± 20.1 y). Eight patients had intestinal dysmotility and eating disabilities due to scleroderma (n = 4) and gastrectomy (n = 4) (6 women and 2 men; mean age: 51.9 ± 19.5 y). Nine patients had had curative treatments for cancer, with no signs of recurrence at the start of HPN (7 women and 2 men; mean age: 61.3 ± 8.5 y). Seven had radiation enteritis, 5 had short bowel, and 4 had both. Three patients had had intestinal resections because of a mesenteric infarction (2 women and 1 man; mean age: 67.2 ± 12.8 y) and a 36-yr-old woman had congenital lymphangiectasia and protein-losing enteropathy.

Remaining intestinal anatomy was deduced from surgical records. Normal small bowel length was given as 350 cm. The remaining colon was described in quartiles, whereby 100% represented an intact colon and 0% represented a total colectomy. Only 4 patients with a remaining small intestinal length < 200 cm had a preserved cecum and ileocecal valve. Only 12 of the 56 patients did not have enterostomies.

Parenteral nutrition and fluids

Energy and electrolyte supplements were adjusted to maintain a normal body weight, hydration, diuresis, and concentrations of plasma albumin and plasma electrolytes. Glucose was supplied as 27% glucose potassium phosphate (The Counties Medicine Registrations Office in Denmark, Copenhagen) or 5%, 10%, 20%, or 50% glucose. Patients were given synthetic amino acids (Vamin 14 or Vamin glucose; Pharmacia, Copenhagen). Electrolytes were given as a hypertonic electrolyte solution containing calcium, potassium, sodium, magnesium, zinc, copper, acetate, chloride, iodide, and glucose. Attempts were made to use “standard” solutions if at all possible (1 L 27% glucose potassium phosphate, 1 L Vamin 14, and 1 L electrolytes daily), but the composition of the HPN solution was often adjusted to meet the patient’s individual requirements. Lipids (10% or 20% Intralipid, Pharmacia) were supplied in separate 500-mL bottles once or twice a week, mainly to patients with large energy demands or poor nutritional status. The rhythm of administration was generally cyclic and nocturnal, but a few patients with large stoma volumes received saline supplements during the day. The recommended infusion time of standard 3-L HPN bags is 10 h. All patients were allowed an unlimited oral intake and were followed at 3-mo intervals in the outpatient nutrition clinic.

Methods

The fatty acid status of the patients was compared with that of 37 control subjects (laboratory and hospital staff members: 10 men and 27 women, aged 25–60 y, mean age: 38.1 ± 10.3 y). Blood samples were taken after an overnight fast between 0800 and 1100 in the morning in both patients and control subjects. Patients receiving intravenous lipids were instructed not to take lipids 48 h before the blood test. Whole blood (10 mL) for fatty acid analysis was collected in EDTA. Patients had blood taken for routine hematologic and biochemical profiles. Body weight and height were measured. Information regarding the parenteral program was confirmed, and patients and control subjects were instructed to fill in a questionnaire regarding skin problems. In 46 of the 56 patients an estimate of habitual dietary energy intake was performed during a subsequent 2-d admission. Patients collected a double portion of all oral intake during a 48-h session using a kitchen balance. After homogenization of the diet, energy content was determined by bomb calorimetry with ±1 g of the freeze-dried 48-h samples ignited in an IKA adiabatic calorimeter (model C 4000 A; IKA-Analysentechnik, Heitersheim, Germany). The last 10 patients, who refused admission to the hospital, were requested to fill out a dietary record of their habitual consumption of food and beverages for a 3-d period. They were told to select a period representative of their common daily eating and drinking habits, to weigh out food components on a kitchen balance, and to measure energy-containing liquids to the nearest 100 mL. The average energy consumption was calculated by a dietitian using the DANKOST computer program (18). The average intakes of 18:2n–6 and 18:3n–3 were not measured in patients or in control subjects.

The energy content in parenteral nutrition was calculated from information given by the manufacturers of the products. Intralipid (10% and 20%) contained 52% 18:2n–6 and 8% 18:3n–3. The triacylglycerol contents were 115 and 230 mmol/L for 10% and 20% Intralipid, respectively. The trilinoleate content was 52.6 and 105.2 g/L and the trilinolenate content was 8.0 and 16.1 g/L for 10% and 20% Intralipid, respectively. Energy contents of the 2 emulsions were 4600 and 8400 kJ/L, respectively. Basic metabolic rates (BMRs) of the patients were calculated with the Harris-Benedict equation as revised by Schofield (19).

Fatty acid analysis

The blood samples for fatty acid analysis were immediately centrifuged at 1000 × g for 10 min and plasma was stored at −20 °C until analyzed. Fatty acid analysis was performed as described earlier (6). The total lipid fraction from plasma samples was extracted according to the method of Folch et al (20). The phospholipid fraction was isolated by thin-layer chromatography and saponified and methylated by using BF₃ (21). The fatty acid methyl esters were analyzed by gas chromatography using a Hewlett-Packard 5890, series II (Hewlett-Packard, Birkerød, Denmark) equipped with a fused silica column (SP2380; 60 m, 0.25 mm internal diameter, Supelco Inc, Bellefonte, PA).

Statistics

Nonparametric testing was performed because observations were not sampled from a population with a normal distribution and the assumptions of equal variances for a parametric test between groups were not met. The strategy for subgroup assignment was planned after the characteristics of the patient population were obtained and the data collection and analyses were not done until subgroup assignment was performed. Subgroup assessment was performed with a nonparametric Mann-Whitney rank sum test or Kruskal-Wallis one-way analysis of variance on
ranks. Dunn’s method was used as the post hoc test for pairwise multiple comparisons. Chi-square and Fisher’s exact test were used to compare frequencies between groups. P values < 0.05 were considered to represent a significant difference between groups. Calculations were performed by using the SIGMASTAT statistical program package (Jandel Corp, Erkrath, Germany).

RESULTS

Patients were divided into 3 groups according to the length of their remaining small intestine: group A, > 200 cm; group B, 100–200 cm, and group C, < 100 cm (Table 1). Each group was further divided into subgroups that either did not receive parenteral lipids (A+0, B+0, and C+0) or did receive lipids (A+1, B+1, C+1, and C+2) as a part of their HPN program; group C+1 specifies patients who received 500 mL 10% or 20% Intralipid once a week, and C+2 those who received 500 mL 20% Intralipid at least twice a week.

Patient characteristics, amounts of parenteral nutrition administered, results of blood tests, and the number of patients with skin problems according to this classification by remaining small intestinal length are shown in Table 1. Only 22 (39%) of the patients received parenteral lipids in amounts 4–59% of their BMR, corresponding to an average supply of 18:2n–6 and 18:3n–3 of 4.1–45.1 and 0.6–6.9 g/d, respectively.

The effect of small bowel length was evaluated by comparisons between patient groups not administered parenteral lipids (A+0 compared with B+0 compared with C+0). Of the measures listed in Table 1, only enteral intake of dietary energy and amounts of parenteral sodium administered differed between these 3 groups. Parenteral energy and volume, duration of HPN, BMR, age, body mass index (BMI), colonic status, and results of ordinary blood tests were not different. The effect of parenteral lipid was evaluated within groups of patients with comparable small bowel lengths, ie, A+0 compared with A+1, B+0 compared with B+1, and C+0 compared with C+1 and C+2. Patients administered parenteral lipids in groups A, B, and C had a significantly higher parenteral energy supply than patients who did not receive parenteral lipids. Furthermore, patients in groups A and B given parenteral lipids had a lower dietary intake of energy.

Skin problems

On the basis of the questionnaires, control subjects and patients were categorized as having skin problems characteristic of dermatitis associated with EFAD—scaling and dryness of the skin—or not. Two of the 37 control subjects reported skin problems (psoriasis). Of the 56 patients, 25 reported that they had had such problems within the past 3 mo. The frequency of patients with skin problems in groups A+0, A+1, B+0, B+1, C+0, C+1, and C+2 are reported in Table 1. Chi-square intergroup analysis did not show a significant difference between the presence of skin manifestations in groups A+0, B+0, or C+0 (P = 0.20). No difference was detected on subgroup analysis of A+0 compared with A+1 (Fisher’s exact test, P = 0.32), B+0 compared with B+1 (Fisher’s exact test, P = 0.25), or C+0 compared with C+1 and C+2 (chi-square test, P = 0.98). A comparison of patients with and without skin problems did not show any significant differences with regard to the patient characteristics given in Table 1.

Fatty acid composition of plasma phospholipids

Concentrations of the main saturated and unsaturated long-chain fatty acids in the phospholipid fraction of plasma, which has been suggested to be the optimal fraction for detection of changes in EFAs because of its high concentrations of polyunsaturated fatty acids, are given in Table 2 (22). A Holman index, the ratio of 20:3n–9 to 20:4n–6, > 0.2 has been suggested as an appropriate cutoff for the diagnosis of EFAD (23). The fatty acid composition of plasma phospholipids of control subjects closely resembled the fatty acid composition seen in a group of patients without fat malabsorption in our Department of Gastroenterology, who were described in a recent study (6).

Biochemical signs of EFAD were evident in the patients receiving HPN compared with healthy control subjects. The concentration of 18:2n–6 was 22.8% in healthy control subjects compared with 11.4% in patients receiving HPN (P < 0.001). Concentrations of all other n–6 fatty acids, including 20:4n–6, the denominator of the Holman index, were higher but total n–6 concentrations were nevertheless lower as a consequence of the dominance of 18:2n–6. The concentration of 18:3n–3 was 0.2% in healthy control subjects compared with 0.1% in HPN patients (P < 0.01). Differences in other n–3 fatty acids were inconsistent, but concentrations of total n–3 fatty acids were lower than in control subjects because of the dominance of 22:6n–3.

Signs of EFAD may, as shown earlier, include elevated concentrations of n–9 and n–7 fatty acids. 20:3n–9 was increased eightfold from 0.1% to 0.8% and was the principal reason for the increase in the Holman index from 0.01 in control subjects to 0.07 in HPN patients (P < 0.001). Total concentrations of n–9 fatty acids were increased because of the increase in 18:1n–9 (oleic acid), which constituted > 90% of the n–9 fatty acids. All n–7 fatty acids were elevated, which more than doubled total n–7 concentrations from 2.3% in control subjects to 4.9% in HPN patients (P < 0.001).

A close inverse correlation (r = 0.98, P < 0.001) between nonessential and essential unsaturated fatty acids was detected (Figure 1). In comparison, there was no significant correlation between 20:3n–9 and 20:4n–6, the respective numerator and denominator of the Holman index (r = 0.15). P > 0.05; Figure 2). When HPN patients with and without skin problems were compared, no differences could be detected regarding the essential and nonessential fatty acid composition of plasma phospholipids (Table 2).

The effect of small bowel length on plasma phospholipids was evaluated by comparing patient groups not given parenteral lipids (A+0 compared with B+0 compared with C+0). 18:2n–6 was 15.5% in patients with > 200 cm preserved small intestine and 9.1% and 9.0% in patients with 100–200 and < 100 cm, respectively, whereas no changes were detected in total n–6 fatty acids. Reduced small bowel length was not associated with any changes in amounts of n–3 fatty acids. Among n–9 fatty acids, only concentrations of 20:3n–9 were significantly higher with reduced small bowel length, whereas amounts of total n–7 fatty acids were higher as a consequence of higher concentrations of 16:1n–7 and 18:1n–7.

The effect of parenteral lipid on plasma phospholipids was then evaluated in subgroups of patients with comparable small bowel lengths, ie, A+0 compared with A+1, B+0 compared with B+1, and C+0 compared with C+1 and C+2 (Table 3). In group A+1, 20:3n–9 was significantly lower than in group A+0 (0.4% and 0.2%, respectively, P < 0.05), whereas 20:2n–9 was significantly higher. In the B groups, no significant differences in plasma phospholipids were observed; however, only 4 patients in this group received lipids. In the C groups, patients receiving parenteral lipids had significantly higher total n–6 fatty acids.
**TABLE 1**

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Group A+0</th>
<th>Group A+1</th>
<th>Group B+0</th>
<th>Group B+1</th>
<th>Group C+0</th>
<th>Group C+1</th>
<th>Group C+2</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 2M, 7F)</td>
<td>(n = 2M, 4F)</td>
<td>(n = 2M, 10F)</td>
<td>(n = 1M, 3F)</td>
<td>(n = 1M, 10F)</td>
<td>(n = 2M, 7F)</td>
<td>(n = 2M, 10F)</td>
<td>(n = 4M, 1F)</td>
</tr>
<tr>
<td>Small intestinal length (cm)</td>
<td>275(250–313)</td>
<td>320(300–350)</td>
<td>142(130–150)</td>
<td>145(130–167)</td>
<td>60(30–98)</td>
<td>40(23–56)</td>
<td>60(51–83)</td>
</tr>
<tr>
<td>Parenteral lipid (MJ/d)</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Energy as a percentage of BMR (%)</td>
<td>0</td>
<td>18 (11–38)</td>
<td>0</td>
<td>11 (9–23)</td>
<td>0</td>
<td>11 (10–12)</td>
<td>19 (18–37)</td>
</tr>
<tr>
<td>Blood test results</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma carbamide (mmol/L)</td>
<td>5.4 (3.9–17.7)</td>
<td>4.7 (4.2–6.6)</td>
<td>7.7 (4.2–11.3)</td>
<td>4.2 (3.3–5.5)</td>
<td>10.4 (6.1–12.2)</td>
<td>6.0 (3.5–7.9)</td>
<td>5.0 (4.6–5.5)</td>
</tr>
<tr>
<td>Plasma creatinine (mol/L)</td>
<td>587 (559–647)</td>
<td>611 (507–646)</td>
<td>539 (436–573)</td>
<td>621 (494–663)</td>
<td>632 (558–698)</td>
<td>630 (588–662)</td>
<td>630 (588–662)</td>
</tr>
<tr>
<td>Plasma potassium (mol/L)</td>
<td>140 (138–141)</td>
<td>141 (138–141)</td>
<td>140 (138–141)</td>
<td>140 (138–141)</td>
<td>140 (139–142)</td>
<td>141 (140–143)</td>
<td>141 (140–143)</td>
</tr>
<tr>
<td>Plasma alanine transaminase (U/L)</td>
<td>20 (14–35)</td>
<td>28 (18–40)</td>
<td>28 (17–33)</td>
<td>92 (46–105)</td>
<td>30 (26–60)</td>
<td>55 (23–91)</td>
<td>43 (14–66)</td>
</tr>
</tbody>
</table>

1 BMR, basal metabolic rate; HPN, home parenteral nutrition.
2 Median; 25th and 75th percentiles in parentheses.
3,5 Group A+0 significantly different from A+1, B+0 significantly different from B+1 (Mann-Whitney rank sum test), and C+0 significantly different from C+1 and C+2 (Kruskal-Wallis one-way ANOVA on ranks); 3 P < 0.05, 5 P < 0.01, 6 P < 0.001.
4 Groups A+0, B+0, and C+0 significantly different from one another, P < 0.05 (Kruskal-Wallis one-way ANOVA on ranks).
DISCUSSION

Biochemical signs of EFAD were evident in this group of 56 patients receiving HPN. Characteristically reduced plasma concentrations of the essential fatty acids 18:2n-6 and 18:3n-3 were paralleled by increased concentrations of the n-9 and n-7 unsaturated fatty acids, thus maintaining total concentrations of unsaturated fatty acids. The median age of the patients was higher than that of the healthy control subjects and gastrointestinal patients with no malabsorption (Table 3), but Holman et al (23) did not show an effect of sex and age on fatty acid composition of human serum lipids.

A relation between the degree of intestinal insufficiency and biochemical signs of EFAD has been shown. A considerable proportion of patients with gastrointestinal diseases resulting in malabsorption of >25–50% of dietary fat not treated with parenteral nutrition had biochemical signs of EFAD (6), but the coexistence of clinical manifestations has not been investigated. This study extended the spectrum of intestinal insufficiency to focus on patients with minimal food and fat absorption, in whom HPN was necessary; the main clinical manifestation of EFAD, skin problems, and changes in plasma phospholipids were investigated. In this study we relied on self-report of skin conditions, which may be problematic because a formal dermatologic evalua-
Patients with Holman

index > 0.2 (%)

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>Group A+0 (n = 9)</th>
<th>Group A+1 (n = 6)</th>
<th>Group B+0 (n = 14)</th>
<th>Group B+1 (n = 4)</th>
<th>Group C+0 (n = 11)</th>
<th>Group C+1 (n = 7)</th>
<th>Group C+2 (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:0</td>
<td>0.4 (0.3–0.4)</td>
<td>0.3 (0.3–0.5)</td>
<td>0.3 (0.3–0.3)</td>
<td>0.4 (0.3–0.4)</td>
<td>0.4 (0.3–0.4)</td>
<td>0.2 (0.2–0.3)</td>
<td>0.3 (0.3–0.3)</td>
</tr>
<tr>
<td>15:0</td>
<td>0.2 (0.1–0.3)</td>
<td>0.2 (0.1–0.2)</td>
<td>0.1 (0.0–0.1)</td>
<td>0.2 (0.1–0.2)</td>
<td>0.1 (0.0–0.2)</td>
<td>0.1 (0.0–0.1)</td>
<td>0.0 (0.0–0.1)</td>
</tr>
<tr>
<td>16:0</td>
<td>30.4 (27.9–31.0)</td>
<td>28.2 (27.4–29.1)</td>
<td>30.3 (30.0–31.9)</td>
<td>30.0 (29.7–31.1)</td>
<td>30.7 (28.6–32.3)</td>
<td>28.3 (27.2–29.1)</td>
<td>27.5 (26.9–28.9)</td>
</tr>
<tr>
<td>18:0</td>
<td>12.8 (12.2–15.6)</td>
<td>14.7 (13.7–15.4)</td>
<td>12.0 (11.4–13.6)</td>
<td>14.0 (12.7–14.7)</td>
<td>13.3 (11.2–14.5)</td>
<td>13.8 (13.2–16.2)</td>
<td>15.3 (14.0–17.3)</td>
</tr>
<tr>
<td>Total saturated fatty acids</td>
<td>44.0 (43.9–44.2)</td>
<td>43.8 (43.3–44.2)</td>
<td>43.5 (42.4–44.1)</td>
<td>44.7 (43.4–44.9)</td>
<td>42.9 (42.4–44.8)</td>
<td>43.6 (43.1–44.5)</td>
<td>43.4 (43.3–44.6)</td>
</tr>
</tbody>
</table>

Total n-6 fatty acids | 13.6 (12.2–19.9) | 13.5 (12.0–14.7) | 17.9 (16.3–25.6)  | 16.0 (13.5–18.5) | 18.4 (17.9–21.1) | 14.3 (11.7–14.8) | 12.9 (11.0–14.3) |

Total n-9 fatty acids | 17.8 (15.2–23.9) | 17.1 (15.9–18.5) | 24.4 (21.3–31.9)  | 20.6 (19.3–23.6) | 24.3 (20.5–28.2) | 19.4 (15.0–21.0) | 16.3 (15.0–18.8) |

Total n-3 fatty acids | 15.5 (12.7–17.2) | 15.6 (14.4–17.6) | 9.1 (6.5–10.4)    | 11.6 (8.1–12.5)  | 9.0 (7.4–11.5)   | 11.0 (8.9–14.5)  | 12.5 (10.9–19.0) |

Total saturated fatty acids | 3.6 (2.8–4.4)    | 3.6 (2.9–4.5)    | 5.5 (4.1–6.5)     | 5.3 (3.9–7.0)    | 5.6 (5.2–6.9)    | 5.1 (3.5–6.2)    | 4.4 (3.3–4.4)    |

Total n-6 fatty acids | 29.3 (26.2–33.0) | 31.7 (29.3–33.9) | 23.6 (18.8–27.4)  | 27.7 (25.4–28.9) | 24.1 (22.7–29.0) | 30.4 (29.3–34.0) | 31.7 (31.0–34.7) |

Total n-3 fatty acids | 5.9 (4.9–7.2)    | 6.0 (5.1–7.6)    | 4.7 (4.4–6.2)     | 5.3 (4.9–5.9)    | 5.1 (4.5–6.0)    | 5.4 (4.5–6.3)    | 5.6 (4.1–7.0)    |

Total unsaturated fatty acids | 54.2 (53.8–55.0) | 54.8 (53.2–55.2) | 54.6 (53.3–55.3)  | 53.8 (53.4–54.5) | 55.2 (53.6–56.1) | 55.1 (54.6–56.3) | 55.4 (54.5–55.3) |

1 Median; 25th and 75th percentiles in parentheses.

2 Group A+0 significantly different from B+0 and C+0 (Kruskal-Wallis one-way ANOVA on ranks); 3 \( P < 0.01 \)

3 Group A+0 significantly different from A+1 and B+0 significantly different from B+1 (Mann-Whitney rank sum test), and C+0 significantly different from C+1 and C+2 (Kruskal-Wallis one-way ANOVA on ranks); 4 \( P < 0.05 \), 5 \( P < 0.01 \).

6 n in parentheses.

Although small intestinal length per se does not take small intestinal function into consideration, it is often used as a predictor of the severity of intestinal failure and thereby of fat malabsorption. In this study, fat intake and absorption were not specifically measured, but patients were divided according to small intestinal length and the amount of intravenous lipid received.

Criticism may be leveled against grouping the patients by small intestinal length because measurement of intestinal length is difficult, making the reliability of surgical reports uncertain. One must realize, however, that measurement of bowel length is easier and more reliable when the bowel is shorter than 200 cm, thereby making the classification into 3 groups rational. One could argue that radiographic measurements of remaining small intestinal length or better functional measurements of intestinal absorption would have improved the study. Radiographic measurements also have inaccuracies, however, especially because the films are two dimensional and the same difficulties arise as with measurements during the operation when the length of remaining intestine exceeds 200 cm (24). Functional measure-
Requirements of essential fatty acids in patients receiving HPN consuming 8 MJ/d, this would correspond to recommendations at a minimum of 3–4% (26). In a healthy person between 0.5% and 7% of total energy intake, with most recommendations for essential fatty acids in patients receiving parenteral nutrition with a Holman index > 0.2; Δ, healthy control subjects. Not done in this study.

When considering the 3 groups of patients who did not receive intravenous lipids (groups A+0, B+0, and C+0), biochemical signs of EFAD were most predominant in patients with the shortest remaining small bowels. Reduced small bowel length may increase fat malabsorption, causing the biochemical changes shown previously in patients with severe fat malabsorption (6, 1, 25). Changes in concentration, however, were only significant for 18:2n-6 and not for 18:3n-3. Compensatory changes in the n-9 and n-7 fatty acids were as described before (6, 25).

In patients with > 200 cm of remaining small intestine, parenteral lipids caused only minor differences in fatty acids of plasma phospholipids when group A+1 was compared with group A+0, although the 18:2n-6 concentration was still considerably lower in both groups than in control subjects. In patients with < 100 cm of remaining small intestine, those receiving parenteral lipids had a higher concentration of total n-6 fatty acids that did not, however, reach the concentration in healthy control subjects. No differences were seen in n-3 fatty acids. The EFAD-associated compensatory increase in the n-9 and n-7 fatty acids was less predominant in these patients than in patients not given lipids. The Holman index was reduced primarily as a consequence of the reduced concentration of 20:3n-9. The small number of patients in the subgroup analyses, however, may limit interpretation. In a recent study by Mascioli et al (17), no relation between remaining small intestinal length and biochemical signs of EFAD, given as the triene-tetraene ratio (Holman index) for plasma phospholipids > 0.2, was found in 12 patients. However, the study differed from our study because intravenous lipid was stopped in their patients until biochemical signs of EFAD occurred. Some of our patients never received lipids.

Daily requirements for 18:2n-6 are unknown. Estimates vary between 0.5% and 7% of total energy intake, with most recommendations at a minimum of 3–4% (26). In a healthy person consuming 8 MJ/d, this would correspond to ≈8 g 18:2n-6/d. Requirements of essential fatty acids in patients receiving HPN depend on the amount of 18:2n-6 in the diet, the ability to absorb ingested fat, the demand for essential fatty acids, and the amount and availability of endogenous stores. Patients receiving HPN may be prone to deficiency in each of these respects. Patients in groups A+1, B+1, C+1, and C+2 had an average parenteral supply of 18:2n-6 of ≈15, 7, 8, and 16 g/d, respectively. However, in none of these groups was the intravenous lipid supply able to increase the plasma phospholipid concentration of 18:2n-6 to a concentration similar to that of control subjects. Patients in these groups may be using infused 18:2n-6 as an energy source, as proposed earlier (16). Although not given continuously, glucose infusion blocks adipose tissue lipolysis and outflow of 18:2n-6 secondarily to high insulin concentrations (27). Parenteral nutrition may thereby affect the fatty acid composition of plasma phospholipids, which may differ from the fatty acid composition of adipose tissues.

In our study population, patients at risk of more pronounced biochemical signs of EFAD were those with < 200 cm of remaining small intestine who were not given intravenous lipids. Thirteen of 14 patients with a Holman index > 0.2 did not receive intravenous 18:2n-6, whereas 1 patient received 7 g 18:2n-6/d. The lack of coherence between biochemistry and clinical outcome may affect the clinical use of intravenous lipids. High doses of intravenous lipid have been claimed to predispose patients to catheter complications (16) and the price of energy supplied by lipids is ≈7 times the price of energy supplied by glucose.

If one wishes to adjust biochemical plasma phospholipid profiles, our study indicates that almost all patients receiving HPN should be supplemented with lipids. Dose recommendations would have to be adjusted according to repeated blood tests, but this study indicates that large amounts of lipids would be required to normalize plasma phospholipid profiles. If, however, one wishes to prevent an increase in the Holman index to a value > 0.2, our study indicates that 500 mL 20% Intralipid once a week was sufficient in all patients, even in those with minimal oral intake and in those with severe small intestinal failure and extended small bowel resections. The lowest minimal dose to prevent biochemical signs of EFAD was not investigated in this study.
study. Mascioli et al (17) investigated the effect of intravenous lipids on the triene-tetraene ratio (Holman index); by increasing the amount of lipids delivered in total nutrient admixtures in biweekly doses, they found that most patients required a minimum of 1 g · kg body wt\(^{-1}\) · wk\(^{-1}\) to correct serologic signs of EFAD, defined as a Holman index > 0.2. The mean weight of patients in our study was ≈55 kg, so this would correspond to 55 g lipid/wk or ≈250 mL 20% Intralipid. In agreement with the findings of Mascioli et al, we found that 12 of 25 patients with < 200 cm of remaining small intestine who did not receive intravenous lipid had a Holman index > 0.2. None of the 13 patients receiving 500 mL 20% Intralipid at least once a week had a Holman index > 0.2, whereas 1 of 3 patients receiving < 500 mL 20% Intralipid/wk had a Holman index > 0.2.

Recommendations regarding lipid dosages in parenteral supplements depend on the degree of correction of plasma fatty acids in the phospholipids one aims at. Lipid dosage adjustments may be performed according to repeated blood tests in individual patients. Prospective studies should focus on cost-effectiveness and clinical outcome.

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