

Lipid peroxidation and antioxidant status in adults receiving lipid-based home parenteral nutrition^{1,2}

Loris Pironi, Enrico Ruggeri, Carola Zolezzi, Lucia Savarino, Elena Incasa, Andrea Belluzzi, Alessandra Munarini, Sandro Piazzi, Maurizio Tolomelli, Arturo Pizzoferrato, and Mario Miglioli

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ABSTRACT

Background: Infusion of lipid emulsions rich in polyunsaturated fatty acids (PUFAs) may increase lipid peroxidation, which is counteracted mainly by superoxide dismutase (SOD) (a zinc-, copper-, and manganese-dependent enzyme), selenium-dependent glutathione peroxidase (Se-GSHPx), and α -tocopherol.

Objective: We investigated lipid peroxidation and antioxidant status in patients receiving home parenteral nutrition (HPN) providing variable amounts of a lipid emulsion rich in PUFAs, and α -tocopherol, zinc, copper, and manganese as recommended by the American Medical Association, and no selenium.

Design: Serum malondialdehyde, plasma α -tocopherol, selenium, Se-GSHPx, PUFAs, and red blood cell Se-GSHPx and SOD were evaluated in 12 patients and in 25 healthy control subjects. Malondialdehyde was also assessed in a group of 40 healthy control subjects.

Results: Patients had significantly higher concentrations of malondialdehyde and SOD and lower α -tocopherol concentrations and selenium nutritional status. Linear regression analysis showed that malondialdehyde was associated with the daily PUFA load ($r = 0.69$, $P < 0.03$) and with plasma α -tocopherol ($r = -0.59$, $P < 0.05$), but stepwise multiple regression analysis confirmed only the association between malondialdehyde and α -tocopherol; plasma α -tocopherol was associated with the daily PUFA load ($r = -0.65$, $P < 0.04$) and with the duration of HPN ($r = -0.74$, $P < 0.02$).

Conclusions: In HPN patients, the peroxidative stress due to lipid emulsions rich in PUFAs is counteracted primarily by α -tocopherol. The dosages of α -tocopherol, zinc, copper, and manganese recommended by the American Medical Association appear sufficient to sustain SOD activity but inadequate to maintain α -tocopherol nutritional status. HPN formulations should be supplemented with selenium. *Am J Clin Nutr* 1998;68:888–93.

KEY WORDS Home parenteral nutrition, lipid peroxidation, antioxidants, superoxide dismutase, glutathione peroxidase, α -tocopherol, vitamin E, malondialdehyde, selenium, polyunsaturated fatty acids, adults, humans

INTRODUCTION

In human subjects there are 2 main defense systems against lipid peroxidation (1). The first involves mineral-dependent

enzymes—superoxide dismutase (SOD) and glutathione peroxidase (GSHPx)—that, in association, control the level of reactive oxygen species (superoxide anion, hydroxyl radicals, and hydrogen peroxide). SOD removes superoxide anion in the mitochondrial compartment, where SOD is a manganese-containing enzyme, and in the cytosolic compartment, where SOD is copper and zinc dependent. SOD disproportionates superoxide to hydrogen peroxide, which is metabolized in both the intracellular compartments by selenium-dependent GSHPx (Se-GSHPx). Superoxide anion can react with hydrogen peroxide to form hydroxyl radical, which reacts with polyunsaturated fatty acids (PUFAs) to generate lipid peroxides. The second defense system is mainly represented by tocopherols (vitamin E), the most active of which is α -tocopherol. Vitamin E interacts directly with lipid peroxides in plasma lipoproteins and cell membranes to neutralize them. Lipid peroxides are labile species that can undergo further enzymatic and nonenzymatic decomposition to give products that include malondialdehyde and volatile hydrocarbons, pentane (produced by the peroxidation of n-6 PUFAs, which are in the linoleic acid family), and ethane (produced by the peroxidation of n-3 PUFAs, which are in the linolenic acid family). Both breath-pentane output (2) and serum malondialdehyde (3) assays are considered sensitive methods to measure in vivo lipid peroxidation in humans.

In adult patients receiving home parenteral nutrition (HPN), high breath pentane associated with low plasma α -tocopherol and selenium concentrations were observed (4). Patients had high plasma Se-GSHPx concentrations, suggesting that increased lipid peroxidation might have been due to subclinical deficiency of α -tocopherol. The same authors showed that the intravenous infusion of a small amount of lipid emulsion rich in n-6 PUFAs induced a significant increase in breath pentane in both HPN patients and in healthy subjects, indicating that intra-

¹From the First Medical Clinic, the Department of Internal Medicine and Gastroenterology, Saint Orsola–Malpighi Hospital, University of Bologna, Italy.

²Address reprint requests to L Pironi, Department of Internal Medicine and Gastroenterology, Saint Orsola–Malpighi Hospital, Via Massarenti, 9, Bologna, Italy. E-mail: Pironi@med.unibo.it.

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venous lipid infusion may be a peroxidative stress (5). Because the amount of α -tocopherol required to protect against lipid peroxidation is considered a function of the amount of ingested PUFAs, it was suggested that HPN patients may receive an inappropriate ratio of α -tocopherol to PUFA, resulting in a relative deficiency of vitamin E.

The appropriate requirements and chemical form of many nutrients to be delivered intravenously to patients receiving HPN remain to be defined (6). Recommended daily intravenous amounts of zinc, copper, manganese, and chromium were established in 1979 by the American Medical Association (AMA) Department of Foods and Nutrition (7). Patients receiving HPN formula without selenium may be at risk of selenium deficiency (8), but, in 1986, a research workshop of the American Society for Parenteral and Enteral Nutrition was unable to reach a consensus concerning guidelines for the parenteral use of selenium (9). Following the recommendations of the AMA Nutrition Advisory Group, the current parenteral vitamin formulations for adults contain ≈ 10 IU α -tocopherol (10). Patients may receive additional amounts of vitamin E with fat emulsions that contain mostly less active non- α -tocopherols (11, 12).

There have been no further studies investigating the problem of lipid peroxidation and the antioxidant status in adult patients receiving HPN. We evaluated the relations between lipid infusion, lipid peroxidation, and antioxidant status in patients receiving HPN as all-in-one, long-term formulas containing variable amounts of a lipid emulsion rich in PUFAs; α -tocopherol, zinc, copper, and manganese in dosages recommended by the AMA; and no selenium.

SUBJECTS AND METHODS

Subjects

Twelve patients (6 men and 6 women) currently followed by the HPN unit of the Department of Internal Medicine and Gastroenterology of the University of Bologna (13) gave their informed consent to be enrolled in the study. All patients were followed as outpatients and were in a stable clinical and nutri-

tional state at the time of the study. Characteristics of the patients and of their HPN regimens are shown in **Table 1**. Patients had a mean (\pm SD) age of 42.1 ± 11.6 y. Body mass index was calculated with Quetelet's formula [wt (kg)/ht² (m)] and basal energy expenditure with the Harris-Benedict formula (14). Eight patients were consuming a free diet orally. Patient 12 was consuming a low-lipid, low-fiber, lactose-free diet. Patient 6 received 500 mL of an oligopeptide enteral formula orally (4180 kJ Peptamen/L; Carnation, Eau Claire, WI). Patient 10 tolerated only small amounts of a fully liquid diet and patient 9 received no food by mouth. Patients 4 and 5 each had a high-output jejunostomy with a remaining jejunum length of 90 and 60 cm and a mean daily stomal loss of 2500 and 5000 mL, respectively. Four patients received the HPN infusion daily and the other 8 patients received it for 3–6 d/wk. Parenteral solutions were infused overnight for 10–12 h. The basic solution consisted of hypertonic dextrose and crystalline amino acids (8.5–10%, Syntamin; Baxter, Trieste, Italy) with added electrolytes and 3 mL of a mixed trace metal solution (Baxter) providing 90 μ mol Zn, 3.6 μ mol Mn, 12.6 μ mol Cu, and 0.154 μ mol Cr. Vitamins (Cernevite, 11.2 mg *all-rac*- α -tocopheryl acetate; Carnation) and lipid emulsion (20% Intralipid; Kabi Vitrum, Pharmacia Upjohn, Stockholm) were added to the solution by the patient just before beginning the infusion. No patient received intravenous selenium. The PUFA load with HPN was calculated on the basis of the fatty acid content of the lipid emulsion reported by the American Hospital Formulary Service, Bethesda, MD (Drug Information, section 40:20), and the American Society of Hospital Pharmacists, 1989: 50% linoleic acid, 9% linolenic acid, 26% oleic acid, 10% palmitic acid, and 3.5% stearic acid (15). Each 500 mL of the 20% lipid emulsion contains 12 mg *RRR*- α -tocopherol, 92 mg *RRR*- γ -tocopherol, and 44 mg δ -tocopherol (12), giving a total of 30.8 mg α -tocopherol equivalents (α -tocopherol equivalent = 1.0, 0.2, and 0.01 mg of α , β + γ , and δ -tocopherol, respectively) (16). The ratio of α -tocopherol to PUFAs in the HPN regimens was calculated by summing the α -tocopherol equivalents in the lipid emulsion with the α -tocopherol content of the multivitamin preparation. The daily nutrient and energy contents, respectively, of the HPN infusion were calculated as

TABLE 1
Characteristics of patients and their HPN regimens¹

Patient and sex	Age	Disease	Intestinal failure	Body wt	BMI	Duration	HPN regimens						Number of infusions per week ²
							Amino acids	Glucose	Lipids	PUFAs	PUFAs	α -toc:PUFAs	
	y			kg	kg/m ²	mo	g/d	g/d	g/d	g/d	% of energy	mg · g ⁻¹ · d ⁻¹	
1, M	32	Crohn	SBS	72	22.1	33	85	200	50	29.5	16	0.90	5 [68]
2, M	16	Infarction	SBS	58	17.3	4	80	200	50	29.5	16	0.90	7 [96]
3, F	45	Infarction	SBS	50	20	72	42	150	50	29.5	21	0.90	7 [105]
4, F	37	Crohn	SBS	58	21.3	51	17	80	45	26.5	18	1	3 [28]
5, M	45	Crohn	SBS	55	20.2	52	42	80	0	0	0	—	4 [20]
6, M	33	Polyposis	Fistulas	64	22.9	30	50	265	50	29.5	15	0.90	6 [97]
7, F	45	Crohn	SBS	41	18.9	64	42	150	50	29.5	21	0.90	5 [82]
8, F	48	Infarction	SBS	55	21.5	64	100	263	100	59	14	0.45	5 [141]
9, M	50	Crohn	Fistulas	57	20.6	78	100	340	50	29.5	12	0.90	7 [169]
10, F	46	Scleroderma	PO	55	19.5	40	75	225	50	29.5	15	0.90	7 [135]
11, F	63	Crohn	SBS	41	16.6	92	80	200	50	29.5	16	0.90	4 [90]
12, M	46	Scleroderma	PO	57	18.6	100	80	300	100	59	24	0.45	5 [128]

¹HPN, home parenteral nutrition; PUFAs, polyunsaturated fatty acids; α -toc, α -tocopherol equivalents; SBS, short-bowel syndrome; PO, pseudo obstruction.

²Percentage of basal energy expenditure in brackets.

follows: g and kJ nutrient infused/kg body wt the night before blood collection; the weekly nutrient and energy contents, respectively, were calculated as follows: g and kJ nutrient infused \cdot d⁻¹ \cdot kg body wt⁻¹ \times (number of infusions/wk)/7. The total energy supplied by the HPN infusion was estimated weekly as a percentage of the basal energy expenditure (BEE): (total kJ provided by HPN/d \times the number of infusions/wk)/(BEE \times 7). The amount of energy provided weekly by the HPN regimen ranged from 82% to 169% of the BEE in 9 patients and was 68% in 1 patient and 20–28% in 2 patients. Thus, the amount of nutrients provided by the oral diet was low or minimal in all but 2 patients (patients 4 and 5; Table 1), who had a disease associated with high malabsorption of fat-soluble vitamins and high intestinal losses of water, minerals, and divalent cations (17).

The control subjects were 25 age- and sex-matched, healthy volunteers (13 men and 12 women) aged 43.4 ± 10.8 y. Eighteen of the control subjects were blood donors and 7 were employees of Saint Orsola Hospital. Serum malondialdehyde was assessed also in a second group of 40 healthy control subjects (16 men and 24 women aged 37 ± 9.3 y).

Blood collection

Blood samples were drawn from healthy, fasting subjects in the morning and from HPN patients 3–4 h after discontinuation of their overnight infusion. For selenium analysis, blood was collected into heparin-containing, metal-free vacutainers (Becton Dickinson and Co, Meylan, France). Blood samples for determination of plasma α -tocopherol, plasma and erythrocyte Se-GSHPx, erythrocyte SOD, and plasma fatty acids were collected in plastic tubes containing tripotassium EDTA. All samples were immediately put on ice and centrifuged ($1000 \times g$, 10 min, 4°C) within 20 min. Plasma was removed and the erythrocyte fraction was washed 3 times with saline and hemolyzed by resuspending it in the original volume with cold, deionized water. Blood for serum malondialdehyde analysis was collected in plastic tubes. Samples of plasma, serum, and hemolysate were appropriately stored until analyzed. Blood for general hematologic analysis, including hemoglobin and plasma cholesterol and triacylglycerol, was collected according to routine procedures and measurements were made immediately after samples were drawn.

Analyses

Plasma selenium concentrations were determined in triplicate with a graphite furnace atomic absorption spectrometer (model 939QZ UNICAM; Solaar, Cambridge, United Kingdom) by using a standard addition method and a deuterium background corrector. Bovine serum with a low selenium concentration was used to prepare the standard curve. Human sera (standard reference material 1598; National Institute of Standards and Technology, Gaithersburg, MD) were used for validating the accuracy and precision of the method. Samples were compared with the standards curve by using the standard curve, linear least squares fit analysis. The detection limit for selenium is $0.093 \mu\text{mol/L}$ (7.4 ng/mL) of diluted specimen.

Se-GSHPx and SOD activities were measured with a Cobas Fara (Roche, Basle, Switzerland) automated spectrophotometer. Plasma and erythrocyte Se-GSHPx were measured with a coupled-enzyme procedure described by Paglia and Valentine (18) by using a commercial diagnostic kit (Ransel; Randox Laboratories Ltd, Ardmore, United Kingdom). Enzyme activity in plasma was reported as U ($1 \mu\text{mol NADPH oxidized per min/L}$ plasma

and in erythrocytes as U/g hemoglobin. SOD activity was measured by using a commercial diagnostic kit (Ransod; Randox Laboratories Ltd). Enzyme activity was reported as U (50% inhibition of the rate of formazan dye formation)/g hemoglobin.

Serum malondialdehyde concentrations were measured as the product generated by the reaction between thiobarbituric acid (TBA) and malondialdehyde (3) and were analyzed by HPLC. To 1 mL serum, 1.5 mL sodium phosphotungstic acid (34 mmol) and 4 mL sulfuric acid (150 mmol) were added. The mixture was centrifuged at $1500 \times g$ for 10 min at room temperature. After the supernate was removed, 2 mL distilled water and 1 mL (600 mg) 2-TBA (Sigma Chemical Co, St Louis) diluted in acetic acid (100 mL, 1 mol/L) were added. After 60 min at 100°C, the tubes were cooled at room temperature and 100 μL HCL was added and the mixture was centrifuged at $1500 \times g$ for 10 min at room temperature. Then, 4 mL butanol was added, the mixture was centrifuged at $1500 \times g$ for 10 min at room temperature and the organic layer was removed for chromatographic analysis. The mobile phase (flow rate, 1 mL/min) was 400 mL methanol and 50 mmol phosphate buffer. Analysis was performed by fluorescence detection (excitation wavelength: 532 nm; emission wavelength: 555 nm) with a fluorometer (Kontron Instruments, St Legier La Chiesaz, Switzerland).

Plasma α -tocopherol was evaluated with reversed-phase HPLC as described previously (19). For the assessment of vitamin E nutritional status, the ratio of plasma α -tocopherol (μmol) to cholesterol + triacylglycerol (mmol) was calculated. Plasma fatty acids were analyzed by gas chromatography as described previously (20). The total plasma PUFA concentration was calculated by summing the plasma phospholipid concentrations of the n-6 PUFAs (linoleic, arachidonic, and docosapentaenoic acids) and the n-3 PUFAs (linolenic, eicosapentaenoic, and docosahexaenoic acids).

Statistical analysis

Data are reported as means \pm SDs. The Mann-Whitney *U* test was used to evaluate the differences between means. The Spearman test and stepwise multiple regression analysis were used to examine the relations. The SPSS/PC computer program (SPSS Inc, Chicago) was used for the analyses.

RESULTS

Mean serum malondialdehyde concentrations were $2.19 \pm 0.82 \mu\text{mol/L}$ in HPN patients, $1.75 \pm 0.41 \mu\text{mol/L}$ in the 25 age- and sex-matched control subjects, and $1.43 \pm 0.35 \mu\text{mol/L}$ ($P < 0.003$ compared with HPN patients) in the second group of 40 healthy subjects (Table 2). HPN patients had significantly lower plasma and erythrocyte concentrations of Se-GSHPx, ratios of plasma α -tocopherol to cholesterol + triacylglycerol, and concentrations of plasma α -tocopherol, selenium, and cholesterol, and higher concentrations of erythrocyte SOD. In HPN patients, plasma Se-GSHPx ($r = 0.84$, $P < 0.008$) and erythrocyte Se-GSHPx ($r = 0.72$, $P < 0.03$) were positively correlated with plasma selenium. No patient had clinical symptoms or signs of vitamin E or selenium deficiency.

Serum malondialdehyde was positively associated with the daily PUFA load (Table 3 and Figure 1). Plasma α -tocopherol was negatively associated with the daily PUFA load, whereas plasma selenium and plasma Se-GSHPx were negatively associated with the weekly loads of PUFAs and energy. No significant



TABLE 2

Blood concentrations in patients receiving HPN and in sex- and age-matched healthy control subjects¹

	HPN patients (n = 12)	Control subjects (n = 25)
Serum malondialdehyde (μmol/L)	2.19 ± 0.82	1.75 ± 0.41
Plasma α-tocopherol (μmol/L)	17.0 ± 6.0 ²	24.6 ± 6.6
Plasma α-toc:chol + triacyl (μmol/mmol)	3.51 ± 1.04 ³	4.04 ± 0.66
Serum selenium (mg/L)	49.1 ± 26.1 ⁴	94.8 ± 16.3
Plasma selenium GSHPx (U/L)	150 ± 88 ^{5,6}	249 ± 89
RBC selenium GSHPx (U/g hemoglobin)	20.7 ± 8.6 ^{5,7}	31.6 ± 8.0
RBC SOD (U/g hemoglobin)	923 ± 173 ⁸	774 ± 89
Σ Plasma PUFA (mol%)	30.7 ± 2.8	29.7 ± 3.8
Plasma cholesterol (mmol/L)	3.52 ± 1.03 ²	4.81 ± 0.88
Plasma triacylglycerol (mmol/L)	1.44 ± 1.05	0.82 ± 0.26

¹ $\bar{x} \pm SD$. HPN, home parenteral nutrition; α-toc:chol + triacyl, α-tocopherol:cholesterol + triacylglycerols; RBC, red blood cell; GSHPx, glutathione peroxidase; SOD, superoxide dismutase; PUFAs, polyunsaturated fatty acids.

^{2-4,6-8}Significantly different from control subjects: ² $P < 0.002$, ³ $P < 0.01$, ⁴ $P < 0.0001$, ⁶ $P < 0.003$, ⁷ $P < 0.0003$, ⁸ $P < 0.006$.

⁵n = 11.

association was observed for plasma PUFAs. Serum malondialdehyde was negatively correlated with plasma α-tocopherol (Figure 2) and with plasma α-tocopherol:cholesterol + triacylglycerol ($r = -0.55$, $P < 0.07$). Plasma α-tocopherol:cholesterol + triacylglycerol was negatively associated with the duration of HPN ($r = -0.74$, $P < 0.02$; Figure 3). No association was observed between serum malondialdehyde and plasma selenium ($r = -0.22$), plasma Se-GSHPx ($r = -0.24$), red blood cell Se-GSHPx ($r = -0.15$), and red blood cell SOD ($r = 0.23$), or between indexes of selenium nutritional status and duration of HPN. Relations between nutrient loads and HPN, antioxidant status, and lipid peroxidation were evaluated considering serum malondialdehyde as the dependent variable. Only plasma α-toco-

pherol was significantly associated with serum malondialdehyde ($r = -0.63$, $P < 0.03$).

DISCUSSION

The results of the present study support the hypothesis that in patients receiving long-term HPN for benign intestinal failure, the degree of lipid peroxidation depends mainly on the intravenous PUFA load and on α-tocopherol nutritional status. Patients had serum malondialdehyde concentrations that were higher than those of the 25 age- and sex-matched healthy control group and of the second group of 40 healthy control subjects. The lack of significant difference between patients and the group of 25 sex- and age-matched control subjects was probably due to a statistical β error, as suggested by the significant difference between HPN patients and the second group of 40 control subjects. Simple correlations showed that serum malondialdehyde was directly associated with the amount of PUFA infused overnight and inversely associated with α-tocopherol nutritional status and that plasma α-tocopherol was inversely associated with the PUFA load. In multiple regression analysis, only plasma α-tocopherol was associated with serum malondialdehyde, indicating that the level of peroxidative stress due to intravenous PUFAs was mainly dependent on vitamin E status. The peroxidative stress may have been due in part to the lipid peroxides contained in the lipid emulsion.

Pitkanen et al (21) measured pentane in the lipid emulsion they used, indicating that lipid emulsions are prone to lipid peroxidation when stored. After infusing preterm infants with a lipid emulsion, they observed increased amounts of pentane in expired breath. After discontinuing the infusion, the elimination of pentane was nonexponential, consisting of a rapid phase probably due to dissolved pentane formed during storage and to a slow phase, reflecting the elimination of pentane produced in vivo. They also found small amounts of malondialdehyde in the emulsion. However, the results of the analysis of TBA reactants in fat emulsions appear questionable because TBA reactants can

TABLE 3

Simple correlations (r) between nutrient loads with HPN and blood variables¹

HPN loads	Serum malondialdehyde	Plasma α-tocopherol	Plasma α-toc:chol + triacyl	Plasma selenium	Plasma GSHPx ²	RBC GSHPx ²	RBC SOD
PUFAs							
(g · kg body wt ⁻¹ · d ⁻¹)	0.69 ³	-0.65 ⁴	-0.50	-0.62 ⁴	-0.58	-0.44	-0.03
(g · kg body wt ⁻¹ · wk ⁻¹)	0.35	-0.50	-0.38	-0.80 ⁵	-0.82 ⁵	-0.56	-0.23
Amino acids							
(g · kg body wt ⁻¹ · d ⁻¹)	0.43	-0.50	-0.08	-0.43	-0.17	-0.15	-0.01
(g · kg body wt ⁻¹ · wk ⁻¹)	0.19	-0.35	-0.03	-0.56	-0.36	-0.31	-0.07
Glucose							
(g · kg body wt ⁻¹ · d ⁻¹)	0.42	-0.15	-0.34	-0.40	-0.44	-0.48	-0.06
(g · kg body wt ⁻¹ · wk ⁻¹)	0.03	0.07	-0.10	-0.49	-0.60 ⁶	-0.61 ⁶	-0.30
Energy							
(kJ · kg body wt ⁻¹ · d ⁻¹)	0.50	-0.39	-0.28	-0.49	-0.51	-0.47	-0.16
(kJ · kg body wt ⁻¹ · wk ⁻¹)	0.22	-0.19	-0.20	-0.59 ⁷	-0.69 ³	-0.50	-0.30

¹HPN, home parenteral nutrition; α-toc:chol + triacyl, α-tocopherol:cholesterol + triacylglycerol; RBC, red blood cell; GSHPx, glutathione peroxidase; SOD, superoxide dismutase; PUFAs, polyunsaturated fatty acids.

²n = 11.

³ $P < 0.03$.

⁴ $P < 0.04$.

⁵ $P < 0.01$.

⁶ $P < 0.06$.

⁷ $P < 0.05$.

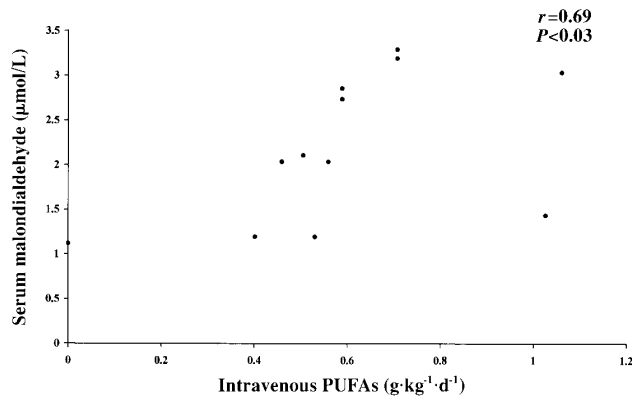


FIGURE 1. Relations between daily amounts of polyunsaturated fatty acids (PUFAs) given with home parenteral nutrition and serum malondialdehyde concentrations.

be generated during the analytic process (22).

The inverse relation between vitamin E nutritional status and the amount of PUFAs infused daily and the progressive decrease of vitamin E status along with the duration of HPN further support previous suggestions to adjust the requirements of intravenous α -tocopherol to the intravenous load of PUFAs. Early studies of patients receiving long-term HPN found plasma α -tocopherol concentrations in the low to normal range, with no clinical manifestation of vitamin deficiency (23). Because vitamin E is transported in plasma lipoproteins, we also based the evaluation of α -tocopherol nutritional status on the ratio of plasma α -tocopherol to lipids, which is considered to reflect vitamin E status better than does plasma α -tocopherol alone (24). This finding agrees with data from Steephen et al (12), who observed in 8 HPN patients that plasma α -tocopherol concentrations were within the normal range and that tissue stores of vitamin E were low on the basis of the ratio of α -tocopherol to cholesterol in adipose tissue. In healthy adults, dietary guidelines recommend an intake of PUFAs equal to 10% of the total energy and an intake of α -tocopherol >0.4 mg/g PUFA, to prevent vitamin E depletion (25). In the HPN regimens we used, the ratio of α -tocopherol to PUFAs was ≈ 0.90 in all but 2 patients, in whom it was 0.45. These ratios did not appear sufficient to maintain vitamin E status in the range observed in the control group, indicating the need for a higher content of α -tocopherol in the HPN formula. However, the PUFA content in the HPN formula was $>10\%$ of the total energy content in most cases. It may be that a PUFA load $<10\%$ of the total energy content decreases the requirement for vitamin E. In this case, the amount of tocopherol supplement recommended by the AMA would be appropriate to maintain vitamin E status.

Selenium nutritional status was lower in patients than in the group of 25 control subjects. The correlation among plasma selenium, plasma Se-GSHPx, and erythrocyte Se-GSHPx concentrations indicated that HPN patients had a biochemical selenium deficiency. Indexes of selenium status were related to the weekly load of nutrients but not to the daily load. Assuming that the weekly nutrient load of the HPN regimen reflects the degree of intestinal failure (intake and absorption of nutrients by the oral route), the inverse correlation between indexes of selenium nutritional status and the weekly nutrient load of the HPN regimen may mirror the degree of absorption of the element by the gas-

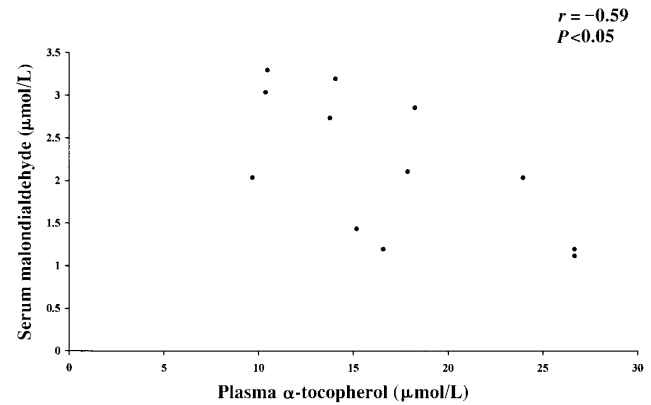


FIGURE 2. Relation between plasma α -tocopherol concentrations and serum malondialdehyde concentrations in patients receiving home parenteral nutrition.

trointestinal tract. Patients had no clinical evidence of low selenium status and the degree of lipid peroxidation did not seem to be affected by the degree of selenium deficiency because there was no correlation between malondialdehyde and indexes of selenium status. The consequences of subclinical selenium deficiency in HPN patients remain to be clarified. The vulnerability of the HPN patients to oxidative stress caused by selenium deficiency may be counteracted by other nutrients participating in the antioxidant system. We observed erythrocyte SOD concentrations that were greater in HPN patients than in the group of 25 control subjects. SOD can be induced rapidly in some conditions, such as exposure to an oxidative stress. Ji et al (26) observed increased heart mitochondrial manganese-SOD activity in selenium-depleted rats. No studies have investigated SOD activity in adult HPN patients with selenium deficiency. Huston et al (27) compared 2 groups of low-birth-weight premature infants receiving total parenteral nutrition. One group was supplemented with selenium and the other was not. No significant difference in white blood cell SOD activity was seen between the groups. Infants had low serum zinc concentrations, suggesting insufficient zinc supplementation, which could have prevented the rise in SOD activity. The increased SOD activity observed in

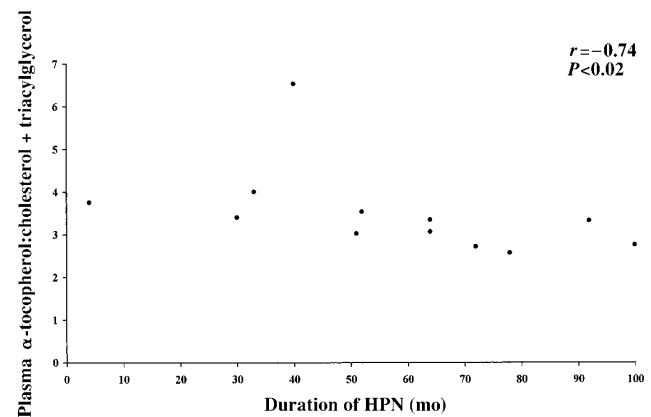



FIGURE 3. Relation between the duration of home parenteral nutrition (HPN) and the ratio of plasma α -tocopherol (μ mol) to cholesterol + triacylglycerol (mmol).



our HPN patients indicated that the zinc, copper, and manganese contents of the HPN regimen were sufficient to sustain an adaptive SOD response to both the peroxidative stress, which was due to the PUFA infusion, and to the selenium deficiency.

In conclusion our results confirm that, in adult patients receiving HPN, the infusion of lipid emulsions rich in PUFAs represents a peroxidative stress that is mainly counteracted by α -tocopherol and indicates that the α -tocopherol content in the current adult parenteral vitamin formulation is inadequate. Furthermore, it appears that most patients requiring HPN should receive HPN formulations that contain selenium, whereas the contents of parenteral zinc, copper, and manganese recommended by the AMA seem sufficient to sustain SOD activity. 

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