Nutrition support and antioxidant defenses: a cause for concern?1–3

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Parenteral nutrition support is widely used in patients with gastrointestinal dysfunction to prevent malnutrition-associated morbidity and mortality (1). Although the efficacy of this therapy in many circumstances remains controversial, it is clear that parenteral nutrition is life saving for patients unable to eat or absorb nutrients for prolonged periods. Clinical studies continue to clarify specific nutrient needs for patients receiving intravenous feeding because there is evidence that current formulations may provide insufficient or, in some cases, excessive amounts of certain nutrients (1, 2).

In this issue of the Journal, Pironi et al (3) examined the effects of parenteral nutrition containing a standard soybean oil–based lipid emulsion on lipid peroxidation, systemic antioxidant enzymes, and plasma antioxidant defenses in the plasma of patients receiving parenteral nutrition. For 3–7 d/wk, patients received parenteral nutrition containing various amounts of an identical lipid emulsion product. The emulsion provided polyunsaturated fatty acids (PUFAs) in amounts ranging from 12% to 24% of intravenous energy (\(\bar{x}\pm SE: 16 \pm 2\%\)). All subjects received a standard intravenous infusion of a vitamin mixture providing 11.2 mg all-rac-\(\alpha\)-tocopherol/d plus 12.8 mg RRR-\(\alpha\)-tocopherol in the lipid emulsion for an average of \(\approx24\) mg/d (3). A selenium-free trace element mixture was also added to the parenteral nutrition solution. All but one subject consumed a free oral diet or small amounts of liquid supplements.

Results showed evidence of peroxidative stress and diminished antioxidant defenses in the plasma of patients receiving parenteral nutrition. Serum malondialdehyde, an index of lipid peroxidation, was 25% higher in patients than in age- and sex-matched control subjects (NS). However, serum malondialdehyde concentrations in patients were 56% higher than those in a separate group of 40 healthy subjects of similar age (\(P < 0.003\)). Plasma \(\alpha\)-tocopherol concentrations were 44% lower in the patients than in healthy control subjects and remained significantly lower (13%) when corrected for plasma lipids. Plasma selenium concentrations were \(\approx50\%\) lower in the parenteral nutrition patients than in control subjects, which correlated with significantly decreased plasma and erythrocyte selenium-dependent glutathione peroxidase (Se-GSHPx) activities. Erythrocyte superoxide dismutase (SOD) activity was significantly higher in patients than in control subjects. No patient had clinical signs or symptoms of vitamin E or selenium deficiency (3).

A peroxidative effect of intravenous PUFAs was suggested by the significant positive correlation between serum malondialdehyde and the daily PUFA load. Furthermore, serum malondialdehyde was negatively associated with plasma \(\alpha\)-tocopherol values. The degree of plasma antioxidant depletion was significantly associated with the daily or weekly PUFA loads. In multiple regression analysis, the peroxidative effects of PUFA infusion (increased malondialdehyde concentrations) were dependent only on plasma \(\alpha\)-tocopherol status (3).

Weaknesses of the study by Pironi et al (3) include the one-time determination of circulating nutrient and antioxidant concentrations and the lack of information on food intake or oral multivitamin-mineral use by the patients and control subjects. Also, it is unknown whether insufficient provision of antioxidant nutrients directly caused increased lipid peroxidation, whether oxidant-mediated stress due to underlying illness or other factors depleted antioxidant nutrient concentrations, or whether both of these situations occurred. Nonetheless, the study is important because it provides new evidence that vitamin E and selenium nutriture may be compromised in adults receiving parenteral nutrition. The vitamin E provided parenterally was not sufficient to prevent increased lipid peroxidation, and plasma \(\alpha\)-tocopherol concentrations appeared to decline as the duration of intravenous feeding increased (3). The amount of \(\alpha\)-tocopherol contained in the daily intravenous multivitamin supplement (11.2 mg) met the amount recommended in the most recent formal guidelines for intravenous vitamin therapy (10 mg) published by the American Medical Association Nutrition Advisory Group > 2 decades ago (4). Also, the intravenous \(\alpha\)-tocopherol dose per gram of PUFA exceeded the value of 0.4 mg vitamin E/g PUFA recommended for healthy subjects consuming oral diets (5).

The authors did not provide intravenous selenium, and plasma concentrations were markedly lower in patients requiring parenteral nutrition than in control subjects. Plasma selenium concentrations were insufficient to maintain the antioxidant enzyme Se-GSHPx at concentrations similar to those of healthy control subjects. Of note, there is no current consensus on guidelines for parenteral use of selenium. The actual requirements for \(\alpha\)-tocopherol and selenium in patients requiring parenteral nutrition

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Oxidative tissue damage undoubtedly contributes to acute and chronic disease processes in many patients receiving parenteral nutrition. It is unclear whether the apparent oxidative stress associated with parenteral nutrition contributes to patient morbidity. In a recent study, infusion of a soybean oil–based lipid emulsion increased plasma indexes of lipid peroxidation with a concomitant decrease in plasma glutathione status in healthy volunteers (16). Inhibition of insulin-mediated glucose uptake in these subjects appeared to be due, in part, to oxidative stress (16). Decreased tissue glucose uptake mediated by oxidative stress may potentially exacerbate hyperglycemia in some patients receiving parenteral nutrition and increase the risk of infection.

The current shortage of intravenous vitamin products in the United States has resulted in elimination or decreased provision of essential micronutrients in many patients receiving parenteral feeding (17). In light of the study by Pironi et al (3) and other published reports, increased clinical and biochemical monitoring for deficiency of α-tocopherol, selenium, and other micronutrients in parenteral nutrition–dependent patients may be prudent.

REFERENCES

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