

the dual-energy system.¹ It would be interesting to determine the effects on stress response and immune function when 20% of the total energy is supplied as ω -6 polyunsaturated fatty acid under different stress conditions in the Asian races.

Furukawa et al. worked on this particular subject with an animal model and clinical research for several years. Their initial studies focused on ω -6 fat emulsion with total parenteral nutrition at different levels of surgical stress.^{9,10,12} In a more recent article published in the current issue,¹³ they selected two groups of patients—an esophagectomy group, which represented severely stressed patients, and a gastrectomy or colectomy group, which represented moderately stressed patients—and investigated the use of 7-d preoperative and 14-d postoperative total parenteral nutrition with and without lipid. As the lipid, the soybean oil emulsion Intralipid accounted for 20% of the total calories. Serum interleukin-6, C-reactive protein, and glucagons were measured to gauge the severity of surgical stress, and concanavalin A- or phytohemagglutinin-stimulated lymphocyte proliferation was measured as an index of cell-mediated immunity. They found an amplified level of interleukin-6 and a decreased level of concanavalin A- or phytohemagglutinin-stimulated lymphocyte proliferation in the group of severely stressed patients using a soybean oil emulsion. Those investigators found that soybean oil emulsion amplifies the stress response and possibly suppresses cell-mediated immune function in severely stressed patients, but not in moderately stressed patients.

In terms of the study of cytokines and stress conditions, two points should be considered. The first is the method used for measuring cytokine levels in experiments involving samples from circulating serum or the supernatant of ex vivo lymphocyte culture. Sometimes, cytokine level differences cannot be detected in serum, even though they are apparent in the supernatant of ex vivo lymphocyte cultures. The second involves the selection of the infusion time before or after the onset of surgical stress. Relatively few studies have reported the effect of lipid emulsion administered after the onset of stress.⁶

The degrees of surgical stress should be differentiated to improve its management. There are many factors that should be considered, such as the extent of surgery, duration of the operation, injury scores, degree of contamination, and serum stress hormone and cytokine levels. The delineation of these parameters with respect to surgical stress is required to adequately understand surgical metabolism and nutrition.

Myung Duk Lee, MD, PhD, FACS
In-Chul Kim, MD, PhD, FACS
Department of Surgery
Kangnam St. Mary's Hospital
The Catholic University of Korea
Seoul, Korea

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PII S0899-9007(01)00792-4

Bioavailability of Microencapsulated Ferrous Sulfate in Milk

Iron deficiency in infancy continues to be a public health problem in most countries around the world. Infants are most susceptible age groups because they have high requirements for growth but consume a diet low in bioavailable iron. Food fortification is the most practical and best long-term method of preventing iron deficiency in this population.¹ Worldwide experience has shown that the success of this type of intervention is due to its relatively low cost and the fact that it does not require the concerted effort or cooperation on the part of the individuals. However, several technical considerations must be considered.² These include the selection of a suitable vehicle that is widely consumed in reasonably constant amounts by the target group and a low cost iron compound with adequate bioavailability. The fortification process should not negatively affect the organoleptic properties of the food or its shelf life. The increasing use of iron-fortified formula and iron-rich weaning foods have decreased iron deficiency anemia among infants in highly developed countries.³ This phenomenon has yet to occur in the rest of the world, where most children younger than 3 y reside. Highly industrialized, fortified food products (infant formulas and weaning foods) are not available to most infants in the world because of their high cost. Iron-fortified milk formulas have been used mainly for the prevention of iron deficiency in infancy.⁴ However, in the undeveloped world, powdered cow's milk with little modification is commonly used because of its lower cost. Unmodified cow's milk has a marked inhibitory effect on the absorption of non-heme iron because of its high concentration of inhibitors of iron absorption. The main inhibitors in cow's milk are casein, calcium, whey protein, and phosphates.⁵⁻⁷ When 10 to 15 mg/L of iron as ferrous sulfate is added to unmodified cow's milk, only 4% to 5% is absorbed.⁸ However, this absorption can be doubled by the addition of 100 mg of ascorbic acid.⁸ Several field studies have demonstrated the efficacy and effectiveness of powdered cow's milk fortified with iron and ascorbic acid in the prevention of iron deficiency in infancy.⁹

Nonetheless, ferrous sulfate, like others ferrous salts, may catalyze fat oxidation and cause an unacceptable flavor and color changes in several foods. When full-fat milk is selected as the vehicle, iron salts can be added safely only to powdered milk

Correspondence to: Manuel Olivares, MD, Institute of Nutrition and Food Technology (INTA), University of Chile, Macul 5540, Casilla 138-11, Santiago, Chile. E-mail: molivare@uec.inta.uchile.cl

sealed in air-tight containers. If iron salts are added to fluid, high-fat milk, lipoperoxidation occurs within hours. Thus, other fortifiers must be considered when fluid whole cow's milk is the selected vehicle. Fluid milk is preferred in some areas of the world where powdered milk has less appeal.

Iron amino acid chelate and microencapsulated ferrous sulfate are fortifiers that could be added to the fluid phase of high-fat compounds such as milk or milk products without inducing prompt peroxidation or rancidity.^{10,11} Further, the inhibitors in milk have a lesser effect on the iron bioavailability of these "protected" iron compounds.^{10,12,13}

In the past 7 y, several studies have been published regarding the properties and bioavailability of ferrous sulfate microencapsulated with lecithin. Studies in mice have shown a significantly lower acute toxicity of microencapsulated ferrous sulfate than of ferrous sulfate.¹⁴ This product is stable to heat processing when it is added to liquid cow's milk. Thermal treatment at 100°C for 30 min (sterilization) does not affect iron bioavailability.¹¹ When the fortified fluid milk is stored in tetra-pack containers, it has a shelf life of more than 6 mo at room temperature.¹¹

In mice, iron absorption of microencapsulated fortified fluid milk is 1.5- to 1.6-fold higher than fluid milk fortified with ferrous sulfate.^{11,14-16} The corresponding figure in rats is 1- to 1.2-fold.^{17,18} In humans, iron bioavailability of fluid whole milk fortified with microencapsulated ferrous sulfate is 9.2% to 10.2%.^{13,19} This percentage of absorption is comparable to the 11.1%, 9.6% to 13.1%, and 11% obtained in cow's milk fortified with ferrous bis-glycine chelate, ferric glycinate, and ferrous sulfate plus ascorbic acid (molar ratio 1:2), respectively.^{8,10,12}

The efficacy of an iron fortification intervention can be predicted from iron bioavailability studies of the fortified food. The efficacy of a fluid whole milk fortified with 15 mg/L of iron as microencapsulated ferrous sulfate in improving iron status was demonstrated in a field study in 17 children with iron deficiency.²⁰

Powdered cow's milk is widely used in nutrition intervention programs. The study by Lysionek et al.²¹ published in this issue of *Nutrition* assessed the bioavailability of microencapsulated ferrous sulfate in powdered whole milk produced from fortified fluid milk. The investigators used the prophylactic method in rats to answer this question. They demonstrated that iron bioavailability is not affected by the short thermal process used in the dehydration process during the production of powdered milk.

In conclusion, fortification of powdered or fluid cow's milk with an iron form such as microencapsulated ferrous sulfate, which is less influenced by inhibiting dietary ligands and has low prooxidants properties, is an appealing strategy to combat iron deficiency in infancy and childhood.

Manuel Olivares, MD

*Institute of Nutrition and Food Technology
University of Chile Santiago, Chile*

PII S0899-9007(01)00786-9

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