New approaches to iron fortification: role of bioavailability studies

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Iron deficiency anemia remains an enormous global problem. Up to half of the children in developing countries and ≈10% of the children in developed countries are estimated to be iron deficient. Iron deficiency leads to impaired physical work performance, cognitive impairment, and adverse pregnancy outcomes (1). Increasing evidence shows that iron deficiency anemia in infants and toddlers can lead to irreversible developmental delays (2).

With some notable exceptions, such as the Women, Infants, and Children program in the United States and the program of iron-fortified milk distribution in Chile, interventions appear to have had relatively little effect on the prevalence of iron deficiency in small children. This is partly due to problems in the sustainability of these approaches but may in part be due to the inadequate bioavailability of the reduced iron used as an iron fortificant in many fortified foods (3). In developing strategies for combating iron deficiency, it is not enough to provide an iron source for the target children. Supplying adequate quantities of poorly bioavailable nutrients will not resolve the nutrient deficiency problem. For example, the Mexican Progresa infant nutrition support program had a relatively small effect on anemia because of the poor bioavailability of iron in the supplement (4). On the basis of bioavailability studies, the Progresa iron source has been changed from reduced iron to ferrous fumarate (S Vilalpando, personal communication, 2004), the same iron compound evaluated in the article by Tondeur et al (5) in this issue of the Journal.

The bioavailability of iron is a function of its chemical form and the presence of food components that either promote or inhibit its absorption. Bioavailability is tightly linked to sensory changes. For example, ferrous sulfate, a common iron fortificant with good bioavailability, has been known to cause fat oxidation and rancidity in cereal flours and leads to the development of unacceptable colors in salt and cocoa powders (6).

Novel approaches are clearly needed to provide bioavailable iron in a form that is acceptable to the target population, inexpensive, largely self-sustaining, and economically viable. Zlotkin et al (7) recently reported success with a new strategy for iron fortification designed for use at home. They described the use of microencapsulated nutrients that can be opened and added directly ("sprinkled") onto various foods. The nutrients are encapsulated with an inert compound that protects them from oxidation and minimizes their organoleptic effects. In a study conducted in Ghana, this supplement significantly decreased the number of infants with iron deficiency and anemia after 2 mo of treatment (7). However, the use of high-dose iron-containing sprinkles without zinc had adverse effects on zinc status.

In their article, Tondeur et al describe the bioavailability of the microencapsulated ferrous fumarate. Their study was performed in small children, the population for whom the sprinkles were designed. The widespread availability of stable isotopes of iron, their lowered cost, and increasing options for sample analysis have led to a situation where it is safe and feasible to conduct such studies in small children. The physiology of mineral absorption in children is often different from that in adults. Therefore, it is not appropriate to use adults rather than children in investigations in which the product is primarily intended for consumption by children.

The results of the study by Tondeur et al included the critical finding that iron absorption from relatively high doses of encapsulated ferrous fumarate is adequate for meeting the daily iron needs of weaning-age infants. However, the fraction absorbed may have been less than would have been achieved by using ferrous sulfate (8).

An important unanswered question is the role of multinutrient fortification of sprinkles and similar products. We found good absorption of both iron and zinc in a multiple micronutrient–fortified beverage in Peruvian schoolchildren (9). However, the dose of iron provided in the beverage (7 mg/serving) was much lower than that in the sprinkles used by Tondeur et al. The iron doses of 30 and 45 mg used in the study by Tondeur et al were close to or exceeded the upper limit for daily iron intake for infants and children (40 mg/d) established by the National Academy of Sciences (1). The potential risks of zinc and other micronutrient deficiencies with this amount of iron fortification are considerable. It is essential that the bioavailability of iron and zinc be assured in a combined product containing much lower doses of each and potentially containing other crucial micronutrients, including vitamin A, vitamin C, and calcium. Such a combined product would ideally be tested in populations having a range of ages and usual diets and different iron status.

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As the scientific evidence supporting the use of fortified foods increases (5, 9), attention must be turned to the challenge of delivering these products to those at greatest need. Partnerships between nongovernmental organizations, industry, and academia are crucial for developing, testing, and ultimately marketing new approaches such as fortified beverages and sprinkles. This is a challenge that cannot be met by any single group or even any single fortification approach.

In the study by Tondeur et al, >3 mg Fe/d was absorbed in children with iron deficiency anemia from the sprinkles containing 45 mg Fe. Sprinkles could be used as therapy for children with known iron deficiency anemia (7). It is important, nonetheless, to keep the tasks of prevention and treatment of anemia separate. Long-term community programs providing iron to at-risk children, even in areas with high incidences of iron deficiency, would likely benefit from iron doses more consistent with dietary recommendations for daily iron intake. However, in many (but not all) situations, even in developing countries, rapid assessment of at least hemoglobin or hematocrit is possible. With the use of such a screen to detect anemic children who are likely to be iron deficient, the long-dreaded, poor-tasting ferrous sulfate syrups and drops could be replaced with high-dose sprinkles.

Meanwhile, it is clear that novel approaches to iron fortification are effective, provide bioavailable iron, and have the potential to contribute substantially to relieving global iron deficiency. Assuring bioavailability is an important stop along the road of further development of this approach.

**REFERENCES**