Journal of Tropical Pediatrics Advance Access published March 3, 2010
JOURNAL OF TROPICAL PEDIATRICS, 2010

Iron Fortification Strategies for the Control of Childhood Anemia in Brazil

by Joel Alves Lamounier,[1] Flávio Diniz Capanema,[2] Daniela da Silva Rocha,[3] Jose Eduardo Dutra de Oliveira,[4] Maite Costa da Silva,[1] *and* Carlos Alberto Nogueira de Almeida[4]

[1]*Faculty of Medicine, Public University of Minas Gerais (UFMG), Belo Horizonte, Minas Gerais, Brazil*
[2]*Faculty of Health and Human Ecology, Vespasiano, Minas Gerais, Brazil*
[3]*Faculty of Nutrition, Public University of Bahia (UFBA), Salvador, Bahia, Brazil*
[4]*University of São Paulo, Ribeirão Preto, São Paulo, Brazil*

Correspondence: Joel Alves Lamounier, Faculdade de Medicina da UFMG, Departamento de Pediatria, Avenida Alfredo Balena 190, Belo Horizonte, MG 30130-100, Brazil. Tel.: +55 31 3409 9640. E-mail <jalamo@medicina.ufmg.br>.

Summary

This article presents data on the fortification of foods, necessary as an important public health approach for the success in reducing anemia. The use of food vehicles, iron salts and their costs, as well as recent work on iron fortification of foods in Brazil are reviewed. Recent research serves as a cornerstone for countries that attempt to implement permanent, long-lasting iron fortification programs aimed at the prevention of anemia considering cultural habits, type of iron salts and at-risk groups.

Key words: anemia, iron deficiency, anemia-fortified food, iron compounds, children.

Introduction

The fortification of foods consists in the addition of complementary nutrients to foods *in natura*. The objective of iron food fortification programs is to increase the dietary iron in foods to prevent and control iron deficiency in at-risk groups [1]. The fortification of foods with iron is a preferred strategy advocated by the World Health Organization. Iron added to foods has been shown to be the most efficient options to control iron deficiency, and studies have shown improvements over a period of 1–3 months in people suffering from this deficiency [2]. Once foods are enriched with micronutrients, such as iron, large, at-risk populations will be reached over long periods without the need of effective individual cooperation [3, 4].

In Latin America, food fortification is widely practiced and can be classified into three program types: mandatory fortification of foods commonly consumed in large parts by the population, such as wheat flour and corn meal; fortification targeting specific groups as in the example of foods consumed by infant and children populations, in this case cereal, powdered milk, biscuits and other industrialized foods; and voluntary fortification, in which the food industry adds iron and other micronutrients to industrialized foods [5]. The magnitude of anemia in Brazil represents a serious public health problem, especially because the short-and long-term effects that anemia can produce on growth in at-risk groups. In this article, this issue was discussed as a Brazilian experience to control and reduce anemia in childhood.

Iron Fortification of Foods in Brazil

In 2001, the Ministry of Health made it mandatory the addition of iron [30% Recommended Nutritional Intake (RNI) or 4.2 mg per 100 g] and folic acid (70% RNI or 150 µg) to milled wheat and corn flour. Federal law now dictates mandatory fortification of iron instead of voluntary fortification by the grain industry. This measure has as its core objective of increasing the accessibility of milled cereal grains with iron and folic acid, consumed by the Brazilian population to reduce the prevalence of iron deficiency and neural tube defects in Brazil [6].

However, iron-fortified wheat flour is not always available or it is consumed in small quantities to be affective by poor children 6–60 months of age [7]. Fortification of specific foods, as part of a complementary diet, has shown to be more effective for the control and prevention of iron deficiency among infants [8]. In addition, and according to Hurrell [9], it is likely that the low levels of elemental iron ($40\,mg\ kg^{-1}$) added to wheat flour would have little impact on iron nutrition, but the much higher levels added to commercial infant cereals ($200–550\,mg\,kg^{-1}$) together with vitamin C, could contribute substantially to the prevention of iron deficiency anemia.

doi:10.1093/tropej/fmq001

Studies in this country on iron fortification of foods, over the last 20 years, have shown promising results in the control and prevention of iron deficiency and anemia in infant and child populations. Unfortunately, only a small number of efficacy and effectiveness trails of iron fortification of foods and liquids conducted in Brazil have been published. Researchers have used various types of food vehicles as well as different iron compounds in attempt to reduce nutritional deficiency, particularly iron deficiency. Table 1 presents a summary of 14 major studies on fortification of foods that have demonstrated positive results in combating iron deficiency or iron deficiency anemia in the Brazilian child population.

Fortification of Milk

Cow's milk presents a small concentration and low bioavailability of iron, and consumption of excessive amounts of fresh or pasteurized cow's milk may be associated with occult intestinal blood loss during infancy, which may also contribute toward increasing the occurrence of anemia in infancy [10]. The frequent use of cow's milk in Latin America, including Brazil, during infancy, and iron fortification of this vehicle is an inexpensive alternative to increasing iron levels in children [11].

Torres *et al.* [11] observed a decrease of 45.8 and 54.8% on anemia prevalence in children in municipal day-care facilities and at public health, respectively, after using powdered whole milk fortified with 9 mg of iron and 65 mg of vitamin C per 100 g of powdered milk, during 6 months. In another study, Torres *et al.* [12] observed that the use of pasteurized cow's milk fortified with iron–amino acid chelate reduced the anemia prevalence in 239 children (6–42 months of age), from 62.3% to 41.8% and 26.4% after 6 months and 1-year of study, respectively. In another study that aimed to evaluate iron fortification of infant formula, Ferreira [13] observed an increase from 10.6 g dl^{-1} to 11.3 g dl^{-1} on mean hemoglobin (Hb) levels of an experimental group (68 infants), which received fortified iron milk formula (1.8 mg ferrous sulfate per 200 ml) during 6 months, in contrast with a control group (43 infants) that received milk formula (0.7 mg iron per 200 ml), resulting in a decrease from 10.6 g dl^{-1} to 10.1 g dl^{-1} on mean Hb levels.

Iron Fortification of Biscuits and Bread Rolls

Some studies were conducted on the effect of bovine Hb-fortified cookies on the Hb levels of 16 iron-deficient preschool children in northeast Brazil [14]. Each child was offered five cookies per day containing 1.25 mg of iron over 3 months as part of their normal school meal program. An evaluation of the total nutrients offered to the children showed an iron intake of just 4.0 mg day^{-1}. Baseline mean Hb was 9.4 ± 2.6 g dl^{-1}, and at 3 months, mean Hb increased to 13.2 ± 0.2 g dl^{-1}. Initial anemia prevalence was 73% and it disappeared at 3 months post-intervention. With the addition of bovine Hb-fortified cookies to the children's diet, total iron intake increased to an average of 8.3 mg (83% of iron Recommended Daily Allowance) at a total cost of US$ 0.50 per child, with no measurable side effects or taste alterations reported.

In a study using iron bis-glycinate chelate, Giorgini *et al.* [15] evaluated 89 preschool children during 6 months. Children received two sweet rolls, twice daily, each one fortified with 2 mg iron bis-glycinate (4 mg day^{-1}) 5 days a week. At baseline, 28% of the children had Hb levels <11.0 g dl^{-1}, and at 6 months 9% of the children persisted anaemic. Mean Hb at baseline was 11.5 g dl^{-1} and, at end, 12.6 g dl^{-1}.

TABLE 1
Summary of studies of iron fortification in Brazil

References	Fortification vehicle	Iron compound	Relative change (%)	Intervention duration (months)
Torres *et al.* (1995)	Powdered milk	Ferrous sulfate + vitamin C	66.4–20.6 (day care); 72.8–18 (health clinic)	6
Torres *et al.* (1996)	Milk	Ferrous bis-glycinate	62.3–26.4	12
Ferreira (2000)	Milk	Ferrous sulfate + vitamin C	63.2–33.8	6
Nogueira *et al.* (1992)	Biscuits	Bovine Hb	75–0	3
Fisberg *et al.* (1998b)	Biscuits and rolls	Ferrous bis-glycinate	32–11	2
Giorgini *et al.* (2001)	Sweet rolls	Ferrous bis-glycinate	62–22	6
Dutra de Oliveira *et al.* (1994)	Drinking water	Ferrous sulfate	58–3	8
De Almeida *et al.* (2005)	Drinking water	Ferrous sulfate + ascorbic acid	45.9–31.1	6
Beinner *et al.* (2005)	Drinking water	Ferrous sulfate + vitamin C	43.2–21	8
De Paula and Fisberg (2001)	Sugar	Ferrous tris-glycinate	38.1–19.7 (group 1); 29.4–19.6 (group 2)	6
Tuma *et al.* (2003)	Manioca flour	Ferrous bis-glycinate	22.7–8	4
Fisberg *et al.* (2003)	Bean flour	Ferric pyrophosphate	13–0	4
Almeida *et al.* (2003)	Orange juice	Ferrous sulfate	60–20	4

Iron Fortification of Potable Drinking Water

The addition of iron to potable drinking water is one alternative to the control and prevention of iron deficiency and anemia. This rather simple method can reach a large part of the Brazilian population at each level of the social-economic stratum by the use of drinking water on a daily basis. Drinking water, other than used for drinking, is commonly used for preparation of foods, which may contribute even more towards increasing iron ingestion [16].

Dutra de Oliveira *et al.* [17] evaluated 31 preschool children aged 2–6 years enrolled in day-care facilities in Ribeirao Preto, Sao Paulo. During 8 months, children consumed iron-fortified drinking water (20 mg iron per l) which resulted in a significant decrease in the prevalence of anemia. At baseline, anemia prevalence was diagnosed in 58% of subjects; at 4 months, 16% continued anemic, and finally, at 8-months post-study intervention, anemia virtually significantly reduced; anemia was present in only 3% of subjects. Mean Hb levels at baseline ($10.6 \pm 1.1\,\mathrm{g\,dl^{-1}}$) increased significantly to $12.1 \pm 1.4\,\mathrm{g\,dl^{-1}}$ at 4 months and $13 \pm 1.1\,\mathrm{g\,dl^{-1}}$ at the end of study.

De Almeida *et al.* [18] conducted a study on 150 children frequenting six day-care centers, in the city of Monte Alto, southeast of Brazil, divided into two groups by drawing lots: Iron-C group (3 day-care centers, $n = 74$) which used water fortified with 10 mg elemental iron and 100 mg ascorbic acid per liter, and comparison group (3 day-care centers, $n = 76$) which used water containing only 100 mg ascorbic acid per liter. A fall in the prevalence of anemia and an increase in mean Hb levels associated with height gain were observed in both groups. This study showed that an increased iron supply by fortification of drinking water is a quite simple strategy of previously demonstrated effectiveness. Also, this study demonstrated that for populations receiving an abundant supply of non-heme iron it is possible to control anemia in a quite simple, safe and inexpensive manner by adding only ascorbic acid to drinking water.

In another study, 160 preschool children from eight municipal day-care facilities benefited from daily consumption of iron (12 g element iron per l) plus ascorbic acid ($90\,\mathrm{mg\,l^{-1}}$) prepared in 20-l plastic water jugs [19]. Mean Hb at baseline and after 8 months of intervention increased significantly from $11.8 \pm 1.3\,\mathrm{g\,dl^{-1}}$ to $12.4 \pm 0.93\,\mathrm{g\,dl^{-1}}$, respectively. The prevalence of iron deficiency determined by Hb levels decreased from 43.2% to 21% at 8 months post-intervention. Fundamentally important to the success of this study was education of the targeted population, which resulted in behavior change and a greater awareness of the importance of combating iron deficiency and anemia by the use of iron-fortified drinking water.

Other Food Options Fortification

In ongoing studies with iron fortification of foods, De Almeida *et al.* [20] evaluated iron fortification of orange juice, rich in vitamin C, which greatly facilitates iron absorption [21]. After 4 months twice-daily consumption of orange juice with iron (10 mg ferrous sulfate per 100 ml of concentrated orange juice), anemia prevalence of 50 preschool children decreased from 60% to 20% and mean Hb level increased from $10.5 \pm 1.7\,\mathrm{g\,dl^{-1}}$ to $11.6 \pm 1.1\,\mathrm{g\,dl^{-1}}$ ($P = 0.00$). In another study, De Paula and Fisberg [22] compared the use of fortified sugar added to orange juice offered to two groups of preschool children during 6 months. The anemia prevalence in both groups decreased 18.4 and 9.8% for an ingestion of 10 and 100 mg of iron per kg of sugar, respectively.

Tuma *et al.* [4] studied the impact of cassava flour enriched with ferrous bis-glycinate in 80 preschool children enrolled in a philanthropic institution in the city of Manaus, where mandioca flour is widely consumed. Anemia prevalence decreased significantly from 22.7 to 8% after 4 months of intervention ($P < 0.05$). In the southeastern region of Brazil, another study demonstrated a significant reduction in the prevalence of anemia in 85 children, 2–5 years of age, which was 13% at baseline and had disappeared in subjects who had received iron-fortified bean flour [23] during 4 months. Unfortunately, milled bean flour represents a greater cost burden and, in addition, is not widely consumed throughout Brazil.

Conclusion

The high prevalence of iron deficiency and anemia in infancy in most regions of Brazil have called attention to an inadequate nutrition, making this a serious public health problem, leading to eventual losses in terms of future growth and productivity at all stages of human development. State and federal governmental health agencies must move forward to prioritize national nutrition agenda that will draft mandatory fortification of food staples for mass consumption. Commitment is urgently needed for program duplication and upscaling of the above summarized experiences of fortification of food and liquids with iron, if developmental and cognitive losses to children are to be avoided in future generations.

References

1. Andrade KC. A fortificação de alimentos com ferro no controle da anemia ferropriva. Revista Brasielira de Ciências da Saúde 2004;II:50–5.
2. Nilson A, Piza J. Food fortification: a tool for fighting hidden hunger. Food Nutr Bull 1998;19:49–60.
3. World Health Organization. Preventing and Controlling Iron Deficiency Anaemia Through

Primary Health Care. A Guide for Health Administrators and Programme Managers. Geneva: WHO, 1989.

4. Tuma RB, Yuyama LKO, Aguiar JPL, *et al*. Impacto da farinha de mandioca fortificada com ferro aminoácido quelato no nível de hemoglobina de pré-escolares [Impact of cassava flour fortified with iron amino acid chelate on the hemoglobin level in pre-schools]. Rev Nutr 2003;16:29–39.
5. Pan American Health Organization. Iron compounds for food fortification: guidelines for Latin America and the Caribbean 2002. Nutr Rev 2002;60(7 Suppl 1): 50–61.
6. Agência Nacional de Vigilância Sanitária. Ferro e ácido fólico enriquecem farinha. http://www.anvisa.gov.br/divulga/noticias/2004/180604.htm (29 May 2009, date last accessed).
7. Beinner MA, Lamounier JA. Recent experience with fortification of foods and beverages with iron for the control of iron-deficiency anemia in Brazilian children. Food Nutr Bull 2003;24:268–74.
8. Assao TY, Silva DG, Ribeiro LC, *et al*. A importância do ferro na saúde e nutrição do grupo materno-infantil. Compacta Nutrição 2004;5:7–22.
9. Hurrell RF. Preventing iron deficiency through food fortification. Nutr Rev 1997;55:210–22.
10. Dallman PR, Siimes MA, Stekel A. Iron deficiency in infancy and childhood. Am J Clin Nutr 1980;33: 86–118.
11. Torres MAA, Souza Queiroz S. Prevenção da anemia ferropriva em nível populacional: uma revisão da literatura dos últimos quinze anos [Prevention of iron deficiency anemia in public health: a fifteen years review of the literature]. Nutrire 2000;19:145–64.
12. Torres MAA, Lobo NF, Sato K, *et al*. Fortificação do leite fluido na prevenção e tratamento da anemia carencial ferropriva em crianças menores de 4 anos [Fortification of fluid milk for the prevention and treatment of iron deficiency anemia in children under 4 years of age]. J Public Health 1996;30:350–7.
13. Ferreira AMA. Prevenção da anemia ferropriva em lactentes que freqüentam creches do município de São Paulo, através de uma fórmula láctea infantil fortificada com ferro. [Thesis] São Paulo (SP): Universidade Federal de São Paulo, 2000.
14. Nogueira NN, Colli C, Cozzolino SMF. Controle da anemia ferropriva em pré-escolares por meio da fortificação de alimento com concentrado de hemoglobina bovina: estudo preliminar [Iron deficiency anemia control in pre-school children by food fortification with bovine hemoglobin: preliminary study]. Cad Saúde Pública 1992;8:459–65.
15. Giorgini E, Fisberg M, De Paula RAC, *et al*. The use of sweet rolls fortified with iron bis-glycinate chelate in the prevention of iron deficiency anemia in preschool children. Arch Latinoam Nutr 2001;51(Suppl 1):48–52.
16. Ferreira JF, Aranda RA, Bianchi MLP, *et al*. Utilização da água potável como veiculo de nutrientes: estudos experimentais com ferro [Use of drinking water as a vehicle of nutrients: experimental studies with iron]. Arch Latinoam Nutr 1991;41:400–8.
17. Dutra-de-Oliveira JE, Ferreira JB, Vasconcellos VP, *et al*. Drinking water as an iron carrier to control anemia in preschool children in a day-care center. J Am Coll Nutr 1994;13:198–202.
18. De Almeida CA, Dutra-de-Oliveira JE, Crott GC, *et al*. Effect of fortification of drinking water with iron plus ascorbic acid or with ascorbic acid alone on hemoglobin values and anthropometric indicators in preschool children in day-care centers in Southeast Brazil. Food Nutr Bull 2005;26:259–65.
19. Beinner MA, Lamounier JA, Tomaz C. Effect of iron-fortified drinking water of daycare facilities on the hemoglobin status of young children. J Am Coll Nutr 2005;24:107–14.
20. De Almeida CAN, Crott GC, Ricco RG, *et al*. Control of iron-deficiency anaemia in Brazilian preschool children using iron-fortified orange juice. Nutr Res 2003;23:27–33.
21. Derman DP, Bothwell TH, MacPhail AP, *et al*. Importance of ascorbic acid in the absorption of iron from infant foods. Scand J Haematol 1980;25:193–201.
22. De Paula RA, Fisberg M. The use of sugar fortified with iron tris-glycinate chelate in the prevention of iron deficiency anemia in preschool children. Arch Latinoam Nutr 2001;51(1 Suppl 1):54–9.
23. Fisberg M, Lima AM, Naufel C, *et al*. Feijão enriquecido com ferro na prevenção de anemia em pré-escolares. Nutrição em Pauta 2003;59:10–18.