Iron-Fortified Rice Is As Efficacious As Supplemental Iron Drops in Infants and Young Children¹,²

Mark A. Beinner,³* Gustavo Velasquez-Meléndez,³ Milene C. Pessoa,³ and Ted Greiner⁴

Abstract

How to improve iron status among infants and young children is of continued concern in low- to middle-income countries, including Brazil. In a double blind, 5-mo, home-based, randomized trial in Brazil, we gave one group of mildly anemic 6- to 24-mo-old children (n = 175) rice fortified with micronized ferric pyrophosphate using the Ultra Rice technology and a placebo solution (URG) and another group identical nonfortified rice and iron drops. We instructed parents on the correct dosage of iron drops and to feed their children rice as they normally would. We measured serum ferritin (SF) and hemoglobin (Hb) concentrations at baseline and at 5 mo. At baseline, the prevalences of iron deficiency and anemia in the total sample were 73.1 and 100%, respectively. At 5 mo, SF and Hb increased in both groups, although the change in the URG was larger (P < 0.01). Adult participants were unable to distinguish cooked fortified rice from unfortified rice in terms of smell, color, or taste. As rice is normally consumed at home, MPF-fortified rice increased iron stores and reduced anemia in a group of mildly anemic children 6–24 mo old. In populations where young children are routinely fed ~100 g of cooked rice daily, fortifying it with iron may improve iron status at least as well as providing free iron drops. J. Nutr. 140: 49–53, 2010.

Introduction

Iron deficiency (ID) is estimated to affect 3.5 billion people, most of whom are young children and women of reproductive age living in developing countries (1). In young children, it can lead to impairment in cognitive performance and growth as well as increased risk of infection and perinatal mortality (2). Population-based studies in several Brazilian regions have found anemia prevalences >30% among young children (3). Data on iron status are more limited, but smaller studies have also found high prevalences of ID anemia (4,5).

The fortification of wheat and maize flour is commonly practiced in many countries as a cost-effective strategy to control and prevent ID (6). Rice, although a very important food staple, is more complex to fortify. One of the available technologies for doing so is the Ultra Rice (Bon Dente International in the USA) cold extrusion process to manufacture simulated rice grains from rice flour and blend a relatively small number of them with natural grains. This technology has been used to fortify rice with micronized ferric pyrophosphate (MFP). MFP is a white, poorly water-soluble iron compound reported to cause few sensory problems that is particularly useful in fortifying white foods. It is less costly than many other iron compounds (7).

We conducted this trial to compare the efficacy of iron-fortified rice with iron drops in improving young child iron status in a part of Brazil where rice is common in the diet of young children.

We wanted to know whether a normal fortified food could improve iron status among mildly anemic children at the highly vulnerable age of 6–24 mo and thus conducted our study under normal real-life conditions.

Participants and Methods

Study area. The study took place from October, 2007 through February, 2008 in the metropolitan region of Belo Horizonte, the state capital of Minas Gerais in southeastern Brazil. This is an urban region with an estimated population of 315,000. The study was conducted under the auspices of the public health agencies of the cities of Vespasiano and Santa Luzia, both characterized as high-population density areas with relatively low incomes. Each city operates 5 health centers and employs over 40 community health workers per center.

Participants. Eligible children were identified from the community health centers’ databases of births in the local districts. To be included in...
the study, children had to be 6–24 mo of age at the time of enrollment and have a hemoglobin (Hb) concentration between 80 and 110 g/L, obtained during a baseline screening. The identification numbers of eligible anemic children were entered into a dataset using SAS software to randomly divide them individually into intervention and control groups. Participants with severe malnutrition (Z-score < −2 for any anthropometric index), chronic illness, physical handicaps, or lack of parental or guardian consent were excluded.

We calculated the sample size based on the assumption of a 10-g/L change in Hb concentration and an associated SD of 13 g/L, representing a large effect size (Cohen’s $f = 0.77$) for ANOVA, assuming a significance level of 0.05 (2-tailed) and a power of 90%. Eighty-two participants per group were required. An additional 14 participants (20%) per group were added to control for potential loss to follow-up or dropouts, for a total of 96 participants per group.

The Ethics Committee at the Federal University of Minas Gerais (UFMG) approved the study protocol on the condition that no group received only a placebo. Local consent to conduct the study in the 2 regional cities was obtained from each Public Health Office, while individual, written consent to participate in the initial screening and, separately, in the study itself, was obtained from each mother or guardian of each child included in the study. Parents were informed that they would be randomly assigned to a group and would receive free rice and free drops, only one of which would be iron fortified.

**Study design.** The study was a randomized, double-blinded efficacy trial, although it was community based, with some features of an effectiveness trial, as described below. We measured biochemical indicators of iron and Hb status among young children living in families who were assigned to 1 of 2 groups. Those in the Ultra Rice group (URG) received 10 kg of free, fortified rice per month, estimated to be adequate in quantity to meet the entire family’s needs. Those in the control group (CG) received an equal quantity of identical but unfortified rice and iron drops. The URG received an equal quantity of identical-looking drops that contained no iron.

To obtain a rough estimate of actual rice intake during the study, a single 24-h dietary intake assessment was conducted with parents of sample children. This was done in a quiet room by trained nutrition students at each district health clinic. To improve estimations of portion sizes, parents or guardians were shown illustrations of the most commonly used utensils, ensuring they could differentiate a teaspoon from a soup-spoon as well as the size and types of ladles. Rice intake estimates were quantified using DietWin software (Porto Alegre, Brazil).

Participants were evaluated at baseline and after a 5-mo period of receiving free rice and drops. Families, health workers, and research personnel were unaware of group assignments. The key to the group assignment code was kept locked in a file cabinet located in the head researcher’s (M.A.B.) office and disclosed only after data analysis was completed.

Similar to typical effectiveness trials, the study was designed to provide a realistic indication of the impact of primary health care workers providing families with free iron drops (the recently adopted government standard of care in Brazil) compared with mandatory iron drops. The URG received an equal quantity of identical-looking drops that contained no iron.

For this purpose, the Duo-Trio Sensory test was applied under Sensory tests. Sensory evaluation of the fortified rice was conducted to identify any organoleptic differences between the fortified and unfortified rice. For this purpose, the Duo-Trio Sensory test was applied under controlled conditions (14) using individual cabins at the UFMG. These cabins were illuminated with white light designed to mask any visual

**Study design.** The study was a randomized, double-blinded efficacy trial, although it was community based, with some features of an effectiveness trial, as described below. We measured biochemical indicators of iron and Hb status among young children living in families who were assigned to 1 of 2 groups. Those in the Ultra Rice group (URG) received 10 kg of free, fortified rice per month, estimated to be adequate in quantity to meet the entire family’s needs. Those in the control group (CG) received an equal quantity of identical but unfortified rice and iron drops. The URG received an equal quantity of identical-looking drops that contained no iron.

To obtain a rough estimate of actual rice intake during the study, a single 24-h dietary intake assessment was conducted with parents of sample children. This was done in a quiet room by trained nutrition students at each district health clinic. To improve estimations of portion sizes, parents or guardians were shown illustrations of the most commonly used utensils, ensuring they could differentiate a teaspoon from a soup-spoon as well as the size and types of ladles. Rice intake estimates were quantified using DietWin software (Porto Alegre, Brazil).

Participants were evaluated at baseline and after a 3-mo period of receiving free rice and drops. Families, health workers, and research personnel were unaware of group assignments. The key to the group assignment code was kept locked in a file cabinet located in the head researcher’s (M.A.B.) office and disclosed only after data analysis was completed.

Similar to typical effectiveness trials, the study was designed to provide a realistic indication of the impact of primary health care workers providing families with free iron drops (the recently adopted government standard of care in Brazil) compared with mandatory iron fortification of rice. The study thus involved no special training or encouragement of health workers to do more than they normally would to ensure adherence to the instructions given to the mothers about giving iron drops to their children, nor were any instructions provided to families to feed any particular amount of rice to the infant or young child.

**Measurement of variables.** At baseline, height and weight were measured using standard techniques (8). Z-scores for height-for-age (HAZ), weight-for-age (WAZ), and weight-for-height (WHZ) were calculated using the EpiInfo program (version 6.0, CDC) and the NCHS/CDC WHO growth reference data (9). Capillary blood samples to test for anemia were taken from a finger prick using aseptic techniques. Hb concentrations were measured immediately with a portable HemoCue B-hemoglobin photometer (Hemocue) by trained health personnel using standardized techniques (10).

Venous blood samples were drawn by trained laboratory technicians from eligible children at baseline and endpoint from the antecubital vein.

Part of the blood was placed into free evacuated tubes protected from light exposure and allowed to coagulate and then serum was separated by centrifugation (10000 × g; 10 min at room temperature) before transporting. The remaining blood sample was placed into a tube containing EDTA as an anticoagulant (Greiner Bio-one). Both samples were preserved in ice-lined cold boxes and transported to the School of Medicine at UFMG within 4 h of being collected. Aliquots for serum ferritin (SF) and C-reactive protein (CRP) measurement were frozen in trace element-free polyethylene dark Eppendorf (1.0 mL) cone-shaped vials at −80°C.

Hb was measured with a Cell Dyn 1800 counter (Abbott Laboratory) on the same day of blood collection. SF was assayed using a solid-phase, 2-site chemiluminescent immunometric assay (Inmulfite 2000, DPC). Samples were assayed in duplicate to measure within-run precision and aliquots of a pooled serum sample were used to measure interassay precision. Human protein-based matrix with preservative control sera were used to assess accuracy and precision, of which the CV was <5%. CRP was measured by nephelometry (Dade Behring). Survey samples were analyzed in 3 separate batches and the intra-batch CV for the assay ranged from 2.9 to 9.1%. The cutoffs used were as follows: anemia was defined as Hb < 110 g/L (11), ID was defined as SF < 12 μg/L (12), and CRP < 10 μg/L at both baseline and 5 mo was required for inclusion in the study (13). All children were dewormed with a single dose of 200 mg albendazole (Teuto) prior to inclusion, expected to keep them worm-free for at least 60 d. In the study area, children 6–59 mo of age received high-dose oral vitamin A capsules weekly (5 mg).

**Iron sources.** Rice grains were extruded from rice flour by a pasta maker under contract with Camil Foods, S.A., Sao Paulo, Brazil. They contained 10.4 mg Fe/g MFP with a mean particle size of ~3.14 μm (Particle Sizing Systems) purchased from AKSELL Química. These grains were blended with local, commercial rice (milled and donated by Camil) at a 2.4:100 blend ratio, calculated to provide 23.4 mg Fe. A total of 6000 kg of iron-fortified rice was stored at the study headquarters for 1 mo before the start of the study.

We fortified the rice at a level likely to lead to approximately equal supplemental iron absorption in both groups. A 10-kg child in the CG would receive ~10 mg Fe/d (a dose of 20 drops of iron solution thrice weekly). Estimating that ferrous sulfate in a supplement might be absorbed about twice as well as MFP in food and that perhaps 10% of the iron in the fortified rice might be lost in preparation, we aimed for a rice fortification level that would deliver ~23 mg Fe/d when 35 g of uncooked rice was consumed per day (our estimate based on an earlier, small-scale diet assessment).

Parents or guardians in the URG were given both fortified rice and 30-ml amber glass screw-cap vials containing an iron-free lemon and orange-flavored placebo solution, which consisted of 22.5 g of sucrose and 15 mL distilled water/30-mL solution.

The CG received identical unfortified rice (which naturally contained 0.057 mg Fe/100 g) and 30-ml amber glass vials with 25 g Fe/L in the form of ferrous sulfate (also containing citric acid, lemon, and orange artificial flavoring and distilled water).

The bags of rice and droppers for both groups had identical labels. Both groups were told to provide 2 drops of solution 3 times weekly/kg of the child’s body weight. No further instructions on treatment were provided by health personnel during the study.

Health workers provided bags of rice and vials to each participant’s home each month. They kept records of empty rice bags and the estimated quantity of any liquid remaining in glass bottles. Parents or guardians of children participating in the study received weekly visits by health workers during the first month of the intervention and fortnightly visits during the remaining 4 mo. The aim of these home visits was mainly to verify that the rice and drops were being consumed and to determine whether there had been any changes in the children’s health.

**Sensory tests.** Sensory evaluation of the fortified rice was conducted to identify any organoleptic differences between the fortified and unfortified rice. For this purpose, the Duo-Trio Sensory test was applied under controlled conditions (14) using individual cabins at the UFMG. These cabins were illuminated with white light designed to mask any visual

Downloaded from https://academic.oup.com/jn/article-abstract/140/1/49/4600429 by guest on 28 November 2018
differences between the tested products. Thirty-seven nontrained evaluators were recruited from the university community (students, workers, and professors).

**Statistical analysis.** Statistical analyses were performed using the EpilNFo (version 6.0; CDC) and SPSS software (version 17.0). Results are expressed as arithmetic means \(\pm SD\), except as indicated. Comparisons between treatments at baseline and mean differences between groups in Hb were normally distributed. Differences in pre- and post-treatment and the sensory tests were compared using Student’s \(t\) test for paired samples and mean differences were compared using the \(t\) test for independent samples. The mean difference in SF concentrations in the 360 children for having Hb $\leq 110$ g/L (11). After obtaining capillary blood for Hb analysis, we excluded, anemic (Hb $\leq 80$ g/L), who were referred to the local hospital for further tests and treatment.

We randomly assigned 196 children to the URG or the CG. Two children died during the study, 9 moved away from the study site and 10 had at least 1 elevated CRP concentration, for an overall loss of 11%. A total of 84 children in the URG and 91 children in the CG completed the trial. Their baseline values did not differ from those of the participants who completed the trial. Fifty children in the URG and 43 children in the CG were still breast-feeding at the start of the study.

Supervisors reported that 100% of the children in both groups consumed the rice daily and a 24-h recall found this to be a mean of 111.9 ± 66.6 g in the URG and 106.3 ± 57.6 g in the CG. Sixty-seven percent and 66% of participants in the URG and CG, respectively, reported giving placebo or iron drops as instructed, 3 d/wk. Parents who were not in adherence gave the children and their family members. Participants reported no unexpected or unacceptable adverse effects in either group or unacceptable tastes, color, or smell of the fortified rice. We further used the Duo-Trio Triangle test in a panel of adults and determined that the cooked, iron-fortified rice was not considerably distinguishable in color, odor, or taste from identical unfortified rice.

In the CG, a 10-kg child receiving the correct dose would have received 23.8 mg of iron thrice weekly (71.4 mg/wk), a comparable absorbed dose to the URG, because they consumed an estimated mean of 23.4 mg/d of iron (for a total of 3.5 g iron during the 150-d trial). This is far above the 8-mg/d Recommended Daily Intake, because the MFP is so poorly absorbed. Indeed, we found that our originally expected absorption level of 3% may have been too high. Based on research on Ultra Rice (16) and similar products (17), we think that only \(-1\text{–}2\%\) of the iron present in the rice was likely to be absorbed, for an

**Results**

**Recruitment, attrition, adherence, and adverse effects.** At baseline, we screened 556 children 6–24 mo of age for this study. After obtaining capillary blood for Hb analysis, we excluded 360 children for having Hb $\geq 110$ g/L and 4 as being severely anemic (Hb $< 80$ g/L), who were referred to the local hospital for further tests and treatment.

Two children died during the study, 9 moved away from the study site and 10 had at least 1 elevated CRP concentration, for an overall loss of 11%. A total of 84 children in the URG and 91 children in the CG completed the trial. Their baseline values did not differ from those of the participants who completed the trial. Fifty children in the URG and 43 children in the CG were still breast-feeding at the start of the study.

Supervisors reported that 100% of the children in both groups consumed the rice daily and a 24-h recall found this to be a mean of 111.9 ± 66.6 g in the URG and 106.3 ± 57.6 g in the CG. Sixty-seven percent and 66% of participants in the URG and CG, respectively, reported giving placebo or iron drops as instructed, 3 d/wk. Parents who were not in adherence gave the children and their family members. Participants reported no unexpected or unacceptable adverse effects in either group or unacceptable tastes, color, or smell of the fortified rice. We further used the Duo-Trio Triangle test in a panel of adults and determined that the cooked, iron-fortified rice was not considerably distinguishable in color, odor, or taste from identical unfortified rice.

In the CG, a 10-kg child receiving the correct dose would have received 23.8 mg of iron thrice weekly (71.4 mg/wk), a comparable absorbed dose to the URG, because they consumed an estimated mean of 23.4 mg/d of iron (for a total of 3.5 g iron during the 150-d trial). This is far above the 8-mg/d Recommended Daily Intake, because the MFP is so poorly absorbed. Indeed, we found that our originally expected absorption level of 3% may have been too high. Based on research on Ultra Rice (16) and similar products (17), we think that only \(-1\text{–}2\%\) of the iron present in the rice was likely to be absorbed, for an

**Sensory tests.** Of the 37 participants who took the Duo-Trio test, 19 identified the sample as being different from the reference sample (iron-fortified rice and identical, nonfortified rice). To arrive at a monochanical comparison significant at the 5% significance level (that is, to indicate that the iron-fortified rice tasted different from the control rice), 24 such responses would have been necessary. Based on a 7-point hedonic verbal scale (where 7 = “very much liked”), means for general liking (URG: 46.4% and CG: 32.3%), and child vomited (often on several occasions) (CG: 20%). These were the only reports of adverse effects from either group.

**Effect of the treatments on anemia and iron status.** The 2 intervention groups did not differ in baseline characteristics for age, Hb, SF, CRP, or the prevalence of ID (Table 1). At baseline, 4.8 and 14.3% were mildly stunted (HAZ \(< -1.0\)), 0 and 8.8% were mildly wasted (WHZ \(< -1.0\)) in the URG and CG, respectively. The groups did not differ in these anthropometric measures at 5 mo.

After 5 mo of treatment, Hb and SF increased in both URG and CG (Table 2; \(P < 0.01\)). Increases in both Hb and SF concentrations were higher in the URG (\(P < 0.01\) for Hb and \(P < 0.02\) for SF). The prevalence of ID decreased from 69.1 to 25% in the URG and from 76.9 to 52.7% in the CG. The prevalence of anemia decreased from 100% at baseline in both groups to 61.9% in the URG and 85.6% in the CG. These changes over time were significant and they differed between the groups (\(P < 0.01\)) (Fig. 1).

**Discussion**

This 5-mo, randomized, double-blinded trial tested in a community setting the impact of consuming iron-fortified rice in children 6–24 mo of age. Rice is a large part of the Brazilian national diet; an annual mean of 74–76 kg of long-grain rice is consumed per capita (15).

Both fortified and unfortified rice were accepted by 100% of the children and their family members. Participants reported no unexpected or unacceptable adverse effects in either group or unacceptable tastes, color, or smell of the fortified rice. We further used the Duo-Trio Triangle test in a panel of adults and determined that the cooked, iron-fortified rice was not considerably distinguishable in color, odor, or taste from identical unfortified rice.

In the CG, a 10-kg child receiving the correct dose would have received 23.8 mg of iron thrice weekly (71.4 mg/wk), a comparable absorbed dose to the URG, because they consumed an estimated mean of 23.4 mg/d of iron (for a total of 3.5 g iron during the 150-d trial). This is far above the 8-mg/d Recommended Daily Intake, because the MFP is so poorly absorbed. Indeed, we found that our originally expected absorption level of 3% may have been too high. Based on research on Ultra Rice (16) and similar products (17), we think that only \(-1\text{–}2\%\) of the iron present in the rice was likely to be absorbed, for an

**Table 1** Baseline characteristics of the children in the groups receiving iron from fortified rice (URG) and from drops (CG)$^1$

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>URG</th>
<th>CG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>13.2 ± 4.3</td>
<td>14.4 ± 5.2</td>
</tr>
<tr>
<td>Boys, %</td>
<td>58.3</td>
<td>85.9</td>
</tr>
<tr>
<td>HAZ</td>
<td>-0.1 ± 1.3</td>
<td>-0.6 ± 1.5</td>
</tr>
<tr>
<td>WAZ</td>
<td>0.9 ± 0.9</td>
<td>-0.7 ± 0.9</td>
</tr>
<tr>
<td>WHZ</td>
<td>1.3 ± 0.8</td>
<td>-0.5 ± 0.6</td>
</tr>
<tr>
<td>Hb, g/d</td>
<td>96 ± 8</td>
<td>96 ± 8</td>
</tr>
<tr>
<td>SF, $\mu$g/d</td>
<td>9.8 ± 6.5</td>
<td>8.5 ± 4.4</td>
</tr>
<tr>
<td>Serum CRP, mg/d</td>
<td>0.2 ± 0.2</td>
<td>0.2 ± 0.2</td>
</tr>
<tr>
<td>Prevalence of ID,$^3$ %</td>
<td>68.1</td>
<td>76.9</td>
</tr>
<tr>
<td>Prevalence of anemia,$^4$</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

$^1$ Values are mean ± SD or percent unless otherwise noted. Groups did not differ (Student’s \(t\) test).

$^2$ Geometric mean ± SD.

$^3$ ID is defined as SF $< 12$ $\mu$g/d (12).

$^4$ Anemia is defined as Hb $< 110$ g/L (11).
FIGURE 1 The prevalence of ID and anemia in children who received fortified rice (URG, n = 84) or unfortified commercial rice with iron drops (CG, n = 91). Both conditions decreased in both groups (paired t-test) and the changes differed between groups (Student’s t-test), P < 0.01.

TABLE 2 Indicators of iron status in children receiving iron from rice (URG) or from drops (CG) 1

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Treatment groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>URG</td>
</tr>
<tr>
<td>n</td>
<td>84</td>
</tr>
<tr>
<td>Hb, g/L</td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>96 ± 0.67</td>
</tr>
<tr>
<td>Final</td>
<td>106 ± 1.1*</td>
</tr>
<tr>
<td>Mean difference</td>
<td>10 ± 0.08*</td>
</tr>
<tr>
<td>SF, µg/L</td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>9.6 ± 0.71</td>
</tr>
<tr>
<td>Final</td>
<td>13.9 ± 0.60*</td>
</tr>
<tr>
<td>Mean difference</td>
<td>4.3 ± 0.63**</td>
</tr>
</tbody>
</table>

1 Values are arithmetic means ± SEM. *Different from CG, P < 0.01 (Student’s t test); **different from baseline, P < 0.01 (paired-samples t test); #Different from CG, P = 0.02 (Mann-Whitney test).

estimated mean of 0.23–0.46 mg Fe/d. At an estimated 6% absorption, correctly dosed ferrous sulfate drops would have provided 1.43 mg Fe thrice weekly, for a somewhat higher mean absorbed quantity of 0.61 mg/d for a 10-kg child.

Iron absorption is complex. Perhaps the iron drops were on average less bioavailable, because a much larger dose of iron was given at each instance than with the fortified rice, which provided small doses much more often. On the other hand, drops may sometimes have been given to children on an empty stomach, something that was impossible by definition for the fortified rice. About two-thirds of families complied with the instructions on giving the iron drops compared with 100% for the fortified rice, because apparently it was eaten daily by all children in the URG.

Hb and SF concentrations increased in both groups, but more so in the URG. In a 7-mo trial of a similar type of fortified rice among school children in India, Moretti et al. (17) observed an effect on SF but not Hb. Although they dewormed the children before and half-way through the trial, they suggested that the lack of impact on Hb may have been due to endemic infections and widespread micronutrient deficiencies. In an earlier efficacy trial of Ultra Rice in Mexico (16), nonpregnant, nonlactating women consumed iron-fortified rice (20 mg Fe/portion) 5 d/wk for 6 mo. Although participants consumed only about one-half the offered rice, a substantial reduction of anemia was reported. The rice in this trial was fortified with a much more expensive, the offered rice, a substantial reduction of anemia was reported.

In this study, iron fortification of rice without an enhancer was shown to significantly improve Hb and iron status in young children. The level of iron used, although high, would be feasible to use in general fortification due to its low level of absorption. Thus, special fortified foods for young children might not be needed to maintain iron status, at least in a setting where rice is consumed daily by young children (~100 g/d of cooked rice). Our findings suggest that the fortification of rice using MFP deserves to be considered as part of any strategy to control ID anemia in rice-eating populations. PATH, a nonprofit organization based in the USA that is commercializing Ultra Rice with local producers and distributors, estimates that fortifying rice with iron in Brazil may increase the cost of rice by no more than 4% (Dipika Matthias, PATH, personal communication). The cost of allowing ID to remain is likely to represent a much higher cost to society (26).

SF is one of the most useful laboratory measures to measure Fe status (18). However, SF increases independently of Fe status in the presence of acute or chronic inflammation. To control for this, we excluded participants having a higher than normal CRP result (an indicator of inflammation) at the beginning or end of the study. A potential limitation of this study was the lack of a measure of body iron stores using the serum transferrin receptor:SF ratio.

In many countries, milling industries commonly restore iron content lost in the production of refined wheat and maize flours (21). Dozens of governments encourage or, like Brazil, mandate higher levels of iron fortification. Voluntary or mandated iron fortification of rice is still rare, however, largely because of the technological challenges in fortifying a white grain eaten whole rather than as flour. Fortification methods for rice have included coating rice kernels with ferrous sulfate (22), the use of cold extrusion (23), rice biofortified with iron via selective breeding (24), and genetically modified rice containing a ferritin gene (25). The present study adds to a growing body of literature suggesting that iron fortification of rice is now both feasible and efficacious in improving the iron status of women (16), school children (17), and now young children in deficient populations.

The Ultra Rice technology is a relatively simple and low-cost way of addressing iron and other micronutrient deficiencies in rice-eating populations. PATH, a nonprofit organization based in the USA that is commercializing Ultra Rice with local producers and distributors, estimates that fortifying rice with iron in Brazil may increase the cost of rice by no more than 4% (Dipika Matthias, PATH, personal communication). The cost of allowing ID to remain is likely to represent a much higher cost to society (26).

In this study, iron fortification of rice without an enhancer was shown to significantly improve Hb and iron status in young children. The level of iron used, although high, would be feasible to use in general fortification due to its low level of absorption. Thus, special fortified foods for young children might not be needed to maintain iron status, at least in a setting where rice is consumed daily by young children (~100 g/d of cooked rice). Our findings suggest that the fortification of rice using MFP deserves to be considered as part of any strategy to control ID anemia in rice-eating populations. We are currently planning studies in Brazil to evaluate the effectiveness of Ultra Rice in a larger community setting in elementary and middle schools.

Acknowledgments
We thank Diego Moretti for valuable technical and editorial suggestions and Dipika Matthias for providing fortification cost estimates. All authors designed the research and analyzed the data. M.A.B., M.C.P., and G.V.M. conducted the research. M.A.B. and T.G. wrote the paper. All authors read and approved the final manuscript.

Literature Cited


