Early response to the effect of iron fortification in the Venezuelan population[1–3]

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ABSTRACT In Venezuela a severe economic crisis beginning in 1983 provoked a progressive reduction of the quality and quantity of food consumed by the low socioeconomic strata of the population. In these strata, which represent ≥ 80% of the Venezuelan population, we had seen a continuous increase in the prevalence of iron deficiency during that recent decade. As a result, in 1993 the Venezuela Government created the Special Commission for Enrichment of Foods. That same year a fortification program began in which precooked yellow and white maize and wheat flours were enriched with 20 and 50 mg Fe (as ferrous fumarate)/kg flour, respectively. The corn flour was also enriched with vitamin A, thiamine, riboflavin, and niacin, whereas the wheat flour was enriched with these same vitamins, except vitamin A. These two cereals represent 45% of the total energy consumed daily by the low socioeconomic strata of the population. A preliminary survey carried out in Caracas in 1994 in a population of 307 children aged 7, 11, and 15 y showed that the prevalence of iron deficiency determined by measuring the serum ferritin concentration and the prevalence of anemia were reduced from 37% and 19%, respectively, in 1992 to 15% and 10%, respectively in 1994. *Am J Clin Nutr* 1996;64:903–7.

KEY WORDS Iron fortification, ferrous fumarate

INTRODUCTION

Iron deficiency is the major nutritional problem affecting 2150 million people throughout the world, being severe enough to cause anemia in 1200 million people (1, 2). The causative factor is the poor bioavailability of iron from cereal-based diets, which are the staple food in many developing countries (3). Strategies for combating iron deficiency include the following: control of parasitic infection, especially hookworm infection; improvement of sanitation; iron supplementation; and iron fortification (4, 5). Of these strategies, iron fortification of basic foods is the most economical and most convenient approach and has the advantage that it does not require a change in the behavior of individuals.

During the period 1960–1985 the Venezuelan population experienced a progressive reduction in the prevalence of iron deficiency because of the improvement in food consumption by the low socioeconomic class and the reduction in the prevalence of hookworm infection in the rural population (6–9). A survey was made between 1978 and 1985 by FUNDACREDESA (Foundation for the Study of National Growth and Human Development) in different socioeconomical strata of the Venezuelan population. It showed that the prevalence of iron-deficiency anemia and iron deficiency in the lower socioeconomic strata was 9% and 29%, respectively, in 1–3-y-old children, and 5% and 23%, respectively, in women of reproductive age (10, 11). A survey carried out in the city of Maracaibo in 1983 among the low socioeconomic strata showed prevalences of 8% for anemia and 26% for iron deficiency in women 15–45-y old (9), which were relatively low for a developing country. The economic crises that started in 1983 with the devaluation of the Venezuelan currency introduced a progressive reduction in the quality and quantity of food consumption by the low socioeconomic strata, characterized by a lower consumption of meat, vegetables and fruits, cereals, grains, and tubers (12).

In 1993 the Venezuelan health authorities started a program to fortify both precooked maize and wheat flours with iron and vitamins. The present study is concerned with the early response to the effect of iron fortification in the Venezuelan population.

SUBJECTS AND METHODS

Fortification of precooked maize flour began in February 1993. The flour contained 50 mg Fe (as ferrous fumarate)/kg plus vitamin A, thiamine, riboflavin, and niacin (**Table 1**). There is no specific survey indicating the prevalence of deficiency of these vitamins, but the yearly food balance sheets prepared by the National Institute of Nutrition noted a progressive reduction of food containing these vitamins and a decrease in the percentage of people meeting the Venezuelan recommended dietary allowances (12, 13). It was expected that these additional vitamins would lessen and prevent overt deficiencies of these nutrients. The fortification of wheat flour began in

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TABLE 1
Enrichment of food vehicle in Venezuela

	Precooked maize flour	White wheat flour
Vitamin A (IU/kg)	9500	—
Thiamine (mg/kg)	3.1	1.5
Riboflavin (mg/kg)	2.5	2.0
Niacin (mg/kg)	51.0	20.0
Iron (mg/kg)[1]	50.0	20.0

[1] As ferrous fumarate.

August of the same year. In this program wheat flour was enriched with 20 mg Fe (as ferrous fumarate)/kg plus thiamine, riboflavin, and niacin (Table 1). The consumption of precooked maize flour per capita was 80 g/d for the total population in 1994. The consumption of wheat flour was 44 g/d as bread and 30 g/d as pasta. The consumption of these two cereals represented 45% of the total energy consumed daily by the population of the low socioeconomic strata (12, 14, 15). The National Hygiene Institute and the National Institute of Nutrition are responsible for the quality and quantity control of the enrichment. FUNDACREDESA and the Nutritional Anemia Laboratory of the Venezuelan Institute of Scientific Research are charged with monitoring the effect of food fortification by means of periodic surveys. The ethical guidelines of FUNDACREDESA, the Instituto Venezolano de Investigaciones Científicas, the Universidad Central de Venezuela, the Instituto Nacional de Nutrición, and the Instituto de Higiene were followed.

Survey

After the conclusion of the Venezuelan Project on Nutrition, which covered the period 1978–1985, FUNDACREDESA started a new nutrition project called "Living conditions of the Venezuelan population." In this new project, yearly national surveys of 7-, 11-, and 15-y-old children were conducted to study longitudinal growth and development. For the present study only children from labor (stratum IV) and lower (stratum V) socioeconomic strata were analyzed: 38% and 42% of the Venezuelan population, respectively (14, 15). Blood samples were taken at random from children at several schools, at public health centers, and at home from each region of the country (ie, 80% of the regions of Venezuela). These children were classified according to age, sex, and the socioeconomic status of their families, following the Graffar method, modified by Méndez-Castellano and Mendez (16). The goal was to obtain a sample size of ≈100 children for each age group from all regions of the country. The number of subjects for hematologic profile in each survey are representative samples. In the Caracas survey for instance, of 392 public schools with a population of 2 900 000, the schools and children were chosen at random. Blood samples taken from the children were to measure several biochemical variables, including blood hemoglobin concentrations (17), packed cell volume, and serum ferritin concentrations (18). This study only addresses the 1989–1990, 1992, and 1994 surveys. In these surveys, the variables used to identify subjects with anemia and iron deficiency were as follows: the cutoff for anemia was a hemoglobin concentration of 115 g/L for 7-y-old children of both sexes, 120 g/L for 11- and 15-y-old females, and 125 and 130 g/L for 11- and 15-y-old males, respectively; the cutoff for iron deficiency was a serum ferritin concentration < 12 μg/L (11). For each ferritin assay, a known sample with low and high ferritin concentrations was used as a control for interplate variability. Between-assay variation was 7.6% and within-assay variation was 5.4%.

Statistical analysis

Calculation of serum ferritin concentrations in total samples from the 1989–1990, 1992, and 1994 surveys of the Caracas population were performed by arithmetic and logarithmic procedures. Chi-square analysis was used to compare the prevalences of iron deficiency and anemia among the surveys, and Student's *t* tests were used to compare ferritin concentrations among subjects of the three surveys.

RESULTS

Quality and quantity control

The maize flour industry in Venezuela comprises 13 mills in which 1.1 million tons of processed maize is transformed into 700 000 tons of precooked maize flour per year. Wheat is mainly imported from the United States and Canada, and wheat flour is processed in 12 mills, which produce 1 million tons per year.

Random samples of commercial flour packages taken from the market by trained persons from the National Institute of Hygiene and Nutrition approximately every 2 mo during 1993, 1994, and 1995 were analyzed in their laboratories. Analysis of the iron content of the 56 samples taken showed that 83% of the samples had 80–120% of the expected value (Table 1). The cost of the micronutrient mixture is < 1% of the market selling price and is completely absorbed by the respective industry. As mentioned in the Introduction, after 1983 the diet consumed by these socioeconomic strata of the Venezuelan population started to deteriorate progressively, qualitatively and quantitatively. The per capita total iron consumption in 1989 and 1992 was 14.3 and 13.0 mg/d, respectively, in stratum IV and 13.0 and 11.3 mg/d in stratum V. As a result of the iron-fortification program the per capita total iron consumption in 1994 increased to 18 mg and 16.9 mg/d in strata IV and V, respectively.

Survey

The prevalence of iron deficiency (determined by measuring the serum ferritin concentration) and the prevalence of anemia (determined by measuring the blood hemoglobin concentration and packed red cell volume) from surveys carried out in 1989–1990 and 1992 are shown in **Table 2**. The samples from these surveys represent all regions of Venezuela. In the 1989–1990 survey the prevalences of iron deficiency and anemia were 14% and 6%, respectively, whereas in the 1992 survey the prevalence of iron deficiency and anemia both doubled and the prevalence of iron-deficiency anemia more than doubled.

The results of statistical analyses of ferritin concentrations, calculated arithmetically and geometrically, for the three surveys from Caracas are shown in **Table 3**. The median arithmetic and geometric values calculated from the logarithm of ferritin concentration in each sample and the result returned to the original value—26 μg/L in the 1989–1990 survey. This value was dramatically lower (15 μg/L) in the 1992 survey and partially recovered to 22 μg/L (compared with the 1989–1990

TABLE 2
Survey of iron deficiency and anemia in children and adolescents in the low socioeconomic strata of the Venezuelan population[1]

Age and sex	Iron deficiency (serum ferritin < 12 μg/L)	Anemia	
		Total	Serum ferritin < 12 μg/L
	%	%	
1989–1990			
7 y (*n* = 298 M+F)	8.4 [25]	5.0 [15]	1.7 [5]
11 y (*n* = 161 M)	14.9 [24]	11.2 [18]	3.7 [6]
11 y (*n* = 245 F)	16.7 [41]	3.3 [8]	2.0 [5]
15 y (*n* = 125 M)	6.4 [8]	2.4 [3]	0.0 [0]
15 y (*n* = 230 F)	21.3 [49]	6.0 [14]	2.6 [6]
Total (*n* = 1059)	13.5 [147]	5.6 [58]	2.0 [22]
1992			
7 y (*n* = 185 M+F)	29.7 [55]	9.7 [18]	3.2 [6]
11 y (*n* = 109 M)	22.9 [25]	22.9 [25]	7.3 [8]
11 y (*n* = 141 F)	31.9 [45]	12.8 [18]	6.4 [9]
15 y (*n* = 80 M)	28.8 [23]	8.8 [7]	2.5 [2]
15 y (*n* = 138 F)	39.1 [54]	11.6 [16]	8.0 [11]
Total (*n* = 653)	30.5 [202][2]	13.2 [84][2]	5.5 [36][2]

[1] *n* in brackets.
[2] Significantly different from number in 1989–1990 survey, $P < 0.05$.

survey) after 1 y of iron fortification. The mean value from the 1992 survey was lower than that from the 1989–1990 survey and was higher than that from the 1994 survey.

The comparison between the 1992 and 1994 surveys of the Caracas population showed a strikingly significant reduction in the prevalence of iron deficiency, from 36.6% to 15.8%, and the prevalence of anemia, from 19.0% to 9.3%. However, the prevalence of iron-deficiency anemia (4.6%), defined as a serum ferritin concentration < 12 μg/L, was not significantly reduced compared with the value (6.3%) observed in 1992 (**Table 4**).

The mean prevalences of iron deficiency in subjects with ferritin concentrations between 12 and 19 μg/L in the 1989–1990, 1992, and 1994 surveys were 19.0%, 26.2%, and 23.3%, respectively; these values were not related to the prevalence of iron deficiency when the cutoff for serum ferritin was 12 μg/L. There were no significant differences among the three cohorts.

The total prevalence of anemia was 3.6%, 19.0%, and 9.3% in the 1989–1990, 1992, and 1994 surveys, respectively. There were 23 cases of anemia in the three surveys in which the serum ferritin concentration was 12–19 μg/L; in 60% of these cases the ferritin concentration was < 15 μg/L and in 91% it was < 17 μg/L. The prevalence of anemia in subjects with a ferritin concentration between 12 and 19 μg/L showed a similar a trend in the three surveys: low when total anemia and iron deficiency was low, as in the 1989–1990 and 1994 surveys, and relatively high in the 1992 survey when total anemia and iron-deficiency anemia were high.

DISCUSSION

For an iron-fortification program to be successful, it is important to select food vehicles that are consumed daily, to select an iron compound that is well absorbed, and to have the ability to control the enrichment (3, 4, 19). The Venezuelan program of nutrient enrichment met all three criteria. Precooked maize flour bread is consumed by the overall population and this target population eats wheat flour as either bread or pasta. It has been shown that iron absorption from ferrous fumarate is similar to that from ferrous sulfate when added to maize or wheat flours (20, 21). The industrial process of preparing flour permits full control of the fortification ingredients.

Ferrous fumarate had been used to fortify flour in Caracas for > 6 mo before the recommendation was made by the Venezuelan Institute for Scientific Research to use it on a national scale. The organoleptic properties of the flour did not change during this period. The only adverse effect observed during the 2 y of the fortification process occurred in two regions of the country in which hard water is used for making maize bread. The families in these two regions bake the bread the night before it is consumed in the afternoon of the next day, either at school or work. They noticed that the bread turned slightly dark the day after it was baked; this organoleptic change was confirmed in the laboratory. Fortunately, the hard water was a factor in these two regions only, affecting <1% of the population of these regions.

The impact of iron fortification on the prevalence of iron deficiency and anemia deserves comment. Comparison of the median ferritin concentrations from the three surveys showed that after 1 y of iron fortification, 62% of the iron reserves that had been dramatically reduced during the period 1989–1990 to 1992 recovered in 1994. This success occurred despite the fact that the diet consumed by this population continued to deteriorate during 1993 and 1994.

The significant striking reduction in prevalence of iron deficiency and anemia is evident from a comparison of the mean of the sex-age groups in the 1992 Caracas survey with the 1994 Caracas survey. The only exception was in the 15-y-old female group, which had only a slight reduction. The reduction in iron reserves and the large increase in prevalence of iron deficiency and anemia during the period 1989–1990 to 1992 was due to the severe reduction in the quality and quantity of the diet consumed by the labor and lower socioeconomic strata of the population. Consumption of meat, eggs, vegetables, dairy products, and fruit gradually decreased by up to an average of 20% because these items had the highest increase in price (W Jaffe, unpublished observations, 1995).

Since 1983, FUNDACREDESA has calculated the cost of a monthly base diet for a family of five (father, mother, and three children aged 1–3, 7–9, and 16–19). This diet contains only locally produced foods and the main food constituents are maize flour, rice, plantain, potatoes, milk, fruit, meats, vegetables, and eggs. The average macronutrient contents are as follows: 9257 kJ energy, 65 g protein, 343 g carbohydrate, and 66 g fat. The monthly cost for the base diet was 1159 bolivars in 1983, 2167 in 1988, 13 345 in 1992, and 27 474 in 1994. During this period the relation of the US dollar to the local currency changed from 4.30:1 in 1983, 55:1 in 1989, 85:1 in 1992, and 170:1 in 1994. Inflation rose by 80% in 1989, by ≈35% between 1990 and 1992, and by 70% in 1993 and 1994.

In terms of purchase power, 21% of the labor stratum families and 33% of the lower-stratum families did not have enough income to buy the base diet indicated above, and 41% of the labor families and 48% of the lower-stratum families received aid via governmental welfare programs. This large increase in the price of the base diet did not correspond to the

TABLE 3
Statistical analysis of ferritin concentration in total samples from the 1989–1990, 1992, and 1994 surveys of the Caracas population

	1989–1990 (n = 499)		1992 (n = 282)		1994 (n = 317)	
	Arithmetic values	Geometric values	Arithmetic values	Geometric values	Arithmetic values	Geometric values
			$\mu g/L$			
$\bar{x}$	30.57	23.18[1]	18.01	13.46	25.20	20.54[2]
SE	0.85	1.03	0.82	1.05	0.86	1.04
Median	26.00	26.00	15.00	15.00	22.00	22.00
95% CI	28.89, 32.25	21.70, 24.76	16.39, 19.64	12.22, 14.83	23.51, 26.89	18.96, 22.25

[1,2] Significantly different from geometric mean in 1992 survey: [1] $P < 0.0001$, [2] $P < 0.0001$.

minimal salary, which increased from 2000 to 8000 bolivars, and the average real wage, which only increased by 20% during this period (22, 23).

Although the commonly accepted cutoff for iron deficiency has been a serum ferritin concentration < 12 μg/L since 1974 (24), several authors in this field have used a cutoff of 12 to < 20 μg/L (25). The prevalence of subjects with a serum ferritin concentration of 12–19 μg/L in 1992 was not significantly different from that in 1994, despite different prevalences in subjects with a ferritin concentration < 12 μg/L, which probably indicates that the prevalence in the group with a concentration of 12–19 μg/L is not entirely related to iron deficiency. However, there was a trend between the prevalence of anemia in the 12–19 μg/L group and the total prevalence of anemia and iron deficiency based on a value of < 12 μg/L.

The prevalence of anemia and iron-deficiency anemia in the 1992 survey was 19% and 6%, respectively, whereas in the 1994 survey it was 9% and 5%, respectively. The differences between prevalence of anemia and iron-deficiency anemia were probably due to infection and to the fact that only one indicator (ie, serum ferritin) was used to identify iron-deficient subjects (1, 26).

There are few examples in the literature of the early effects of iron-fortification programs (19, 27). Garby and Areekul (28) reported the effects of the fortification of fish sauce with NaFe-EDTA in a Thai village for 1 y. The fortification produced an additional intake of ≈10 mg Fe/d and after 1 y the packed cell volume increased ≈1.5% compared with the control population (27). In a trial of iron fortification in three Central America communities, sugar was the food vehicle enriched with NaFe-EDTA; the additional intake provided ≈3

TABLE 4
Survey of iron deficiency and anemia in children and adolescents in the labor and lower socioeconomic strata of the Caracas population[1]

	Iron deficiency		Anemia		
	<12 μg/L	12 ≤ 20 μg/L	Total	Serum ferritin	
Age and sex				<12 μg/L	12 ≤ 20 μg/L
	%		%	%	%
1989–1990					
7 y (n = 106 M+F)	12.3 [13]	21.7 [23]	0.9 [1]	0.0 [0]	0.0 [0]
11 y (n = 100 M)	12.0 [12]	20.0 [20]	8.0 [8]	2.0 [2]	1.0 [1]
11 y (n = 123 F)	17.9 [22]	18.7 [23]	4.1 [5]	2.4 [3]	0.0 [0]
15 y (n = 52 M)	9.6 [5]	13.4 [7]	0.0 [0]	0.0 [0]	0.0 [0]
15 y (n = 118 F)	18.6 [22]	21.2 [25]	5.0 [6]	1.7 [2]	1.7 [2]
Total (n = 499)	14.1 [74][2]	19.0 [98]	3.6 [20][2]	1.2 [7]	0.6 [3]
1992					
7 y (n = 72 M+F)	36.1 [26]	25.1 [18]	13.9 [10]	4.2 [3]	4.2 [3]
11 y (n = 39 M)	25.6 [10]	33.3 [13]	30.7 [12]	7.7 [3]	5.1 [2]
11 y (n = 52 F)	50.0 [26]	32.7 [17]	23.1 [12]	5.8 [3]	5.2 [3]
15 y (n = 51 M)	31.4 [16]	17.7 [9]	9.8 [5]	5.8 [1]	3.8 [2]
15 y (n = 68 F)	39.7 [27]	22.1 [15]	17.6 [12]	10.3 [7]	2.9 [2]
Total (n = 282)	36.6 [105][3]	26.2 [72]	19.0 [51][3]	6.3 [17]	4.3 [12]
1994					
7 y (n = 91 M+F)	13.2 [12]	24.2 [22]	3.3 [3]	1.1 [1]	3.3 [3]
11 y M (n = 65 M)	12.3 [8]	20.0[13]	15.4 [10]	6.2 [4]	3.1 [2]
11 y F (n = 65 F)	7.7 [5]	33.9 [22]	10.8 [7]	3.1 [2]	4.6 [3]
15 y M (n = 30 M)	3.3 [1]	23.3 [7]	3.3 [1]	3.3 [1]	0.0 [0]
15 y F (n = 66 F)	36.8 [24]	15.2 [10]	13.6 [9]	9.1 [6]	0.0 [0]
Total (n = 317)	15.8 [50]	23.3 [74]	9.3 [30]	4.6 [15]	2.2 [8]

[1] n in brackets.
[2] Significantly different from total for 1992 in same column, $P < 0.05$.
[3] Significantly different from total for 1994 in same column, $P < 0.05$.

mg Fe/d. After 20 mo they found a significant increase in the serum ferritin concentration in the population of all three communities (27–29). Finally, in a South African iron-fortification trial, curry powder was fortified with NaFe-EDTA and tested in an urban Indian community whose daily intake of iron via fortification was 7 mg. After 1 y there was a significant increase in hemoglobin concentration to a mean of 15 g/L and in ferritin to a mean of 15 μg/L (27, 30, 31).

Although the daily iron intake from fortification in our communities was ≈6 mg Fe as ferrous fumarate, which is about one-half as bioavailable as NaFe-EDTA, the striking reduction in prevalence of iron deficiency in the Venezuelan program of iron fortification is very promising. These results, however, should be considered as only an approximation of the effect of iron fortification on the prevalence of iron deficiency in the Venezuelan population because of the small number of subjects tested and the limited age groups studied, and because the results are based only on the population in Caracas. A survey of the entire Venezuelan population will be started in 1996, including vulnerable and nonvulnerable age groups, and will provide more exact data. Investigations carried out in 1995 showed that vitamin A in precooked maize flour prevents the inhibitory effect of phytates contained in the flour, and therefore the absorption from iron-fortified food and iron-containing food is doubled (32).

As far as we know ours is the first iron-fortification trial to be carried out on a national scale in a developing country.

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