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The use of sweet rolls fortified with iron bis-glycinate chelate in the prevention of iron deficiency anemia in preschool children

Giorgini E., Fisberg M., De Paula RAC., Ferreira AMA., Valle J., Braga JAP.

Health and Nutrition Research Center, San Marcos University, Brazil.- Federal University Sao Paulo and State University of Rio de Janeiro, Brazil

SUMMARY. The effectiveness of bread fortified with iron bis-glycinate chelate for the control of iron deficiency and iron deficiency anemia was evaluated in 89 preschool children from families of low socioeconomic level attending 2 day nurseries of the Sao Paulo City Council. During the intervention's time of 6 months the children received besides their usual center's diet, a daily supplement of two sweet rolls fortified with 2 mg each of iron from the chelate for a total daily iron intake of 4 mg. After six months of intervention there was a significant decrease in the prevalence of iron deficiency anemia from 62 to 22%. There was a mean hemoglobin improvement of 1.1 g/dL, and in children with initial hemoglobin levels < 11 g/dL the mean increase in hemoglobin was 1.42 g/dL. The total mean plasma ferritin values increased from 11.34 to 20.2 µg/L, and in those children originally iron depleted the ferritin values normalized. A significant increase in the "z" score for weight/height was also observed. We concluded that the use of sweet rolls fortified with 2 mg of iron from the bis-glycinate chelate is highly effective for the control of iron deficiency and iron deficiency anemia in young children.
Key words: Ferrochel, bread fortification, flour fortification, Ferrochel effectiveness in bread, evaluation of bread fortification.

RESUMEN. Uso de bollos fortificados con hierro bis-glicinato quelado en la prevención de anemia por deficiencia de hierro en preescolares. La efectividad del pan fortificado con hierro bis-glicinato quelado para el control de deficiencia de hierro y la anemia ferropriva en infantes fue evaluada en 89 niños preescolares procedentes de familias de bajo nivel socio-económico, que asistían a hogares de día de la municipalidad del Estado de Sao Paulo, Brazil. La intervención duró 6 meses durante los cuales los niños del estudio recibieron dos bollos fortificados con 2 mg de hierro del quelado cada uno. Después de 6 meses de intervención, se observó una disminución significativa en la prevalencia de anemia ferropriva de 62 a 22%. Hubo una mejoría en los niveles de hemoglobina de 1.1 g/dL en el grupo total, y en aquellos niños que al principio mostraban valores <11 g/dL el aumento medio en hemoglobina fue de 1.42 g/dL. Los valores medios de ferritina en plasma aumentaron de 11.34 a 20.2 µg/L, y todos los niños con depauperación de hierro normalizaron sus niveles de ferritina plasmática. Al final de la intervención se demostró un aumento significativo en el valor de "z" para peso/talla. Se concluye que el consumo de los bollos fortificados con 2 mg de hierro del bis-glicinato quelado por unidad es altamente efectivo en el control de la deficiencia de hierro y la anemia ferropriva.
Palabras clave: Ferrochel, fortificación de pan, fortificación de harina, efectividad de Ferrochel en pan, evaluación de fortificación de pan.

INTRODUCTION

Mineral and vitamin nutritional deficiencies resulting from inadequate diets affect nearly two thirds of the world's population. Iron deficiency is the most prevalent deficiency and the main cause of nutritional anemias affecting almost 2,5 billion people in the world (1,2).

Studies have shown that iron deficiency is responsible for 80% of all nutritional anemias affecting children, and that 59,1% of the world's population is affected by iron deficiency anemia.

Although iron deficiency anemia is more prevalent in developing countries, it also affects industrialized countries where 8% of the population suffers from the disease. It is estimated that in developing countries, nearly 26% of men and 50% of women and children suffer from anemia. In industrialized countries 10% of children less than one year of age suffer from anemia, whereas in developing countries this figure can reach 30 to 80% (3,4).

In Brazil, iron deficiency anemia is considered a public health problem. Data from the National Epidemiology Division show that 1,3% of the total deaths in children result from anemia. In children under 5 years of age, and in women of childbear- bearing age, 50% of the total number of deaths is associated with iron deficiency anemia (5).

Studies carried out during the two last decades have shown a prevalence of more than 50% in the areas investigated (6-9).

An inadequate diet is the main cause of iron deficiency, either because of its quality, or because of the insufficient amount of this micronutrient available in the population diet.

In 1988, Tudisco (10) examined the diets of Latin American countries and found, that in most places, including Brazil, the iron consumed came predominantly from non heme sources, and that the total amount ingested was below the recommended dietary intake (RDI). This fact confirmed dietary deficiency as the main cause of iron deficiency anemia in the populations studied.

Iron deficiency effects go beyond impairments in hemoglobin synthesis affecting besides other organic functions, causing behavioral alterations, reduced physical and intellectual performance, immunity and growth (11,12).

In the last decades, controlling iron deficiency anemia has been an important goal to achieved by any one concerned in solving the nutrition problems that affects large portion of the world population. In 1992, the International Conference on Nutrition held in Rome, attended by representatives of 160 countries, including Brazil, reached what was called a goal-compromise to reduce iron deficiency anemia in pregnant women to 1/3 of the prevalent at that time (3).

The World Health Organization (WHO) suggested that the disease be controlled by nutritional education programs combined with strategic actions to increase iron consumption of the populations at risk. This included iron supplementation and food fortification with iron (13).

Some studies on food fortification have shown promising results, leading many investigators in the world to believe that this is the most effective measure to be taken to prevent and control iron deficiency anemia (14-21). Fortification is defined as the addition of nutrients to food. It is a public health measure of rapid application, but it requires the selection of foods that are commonly consumed by the target population in relatively constant amounts, and to which de micronutrient in deficit can added without altering its organoleptic characteristics (22), and without significantly increasing its cost to be consider as a viable public health measure. The main criteria in selecting the nutrients are: proven need, safety and effectiveness. The effectiveness of the measure is, of course, directly connected to the selection of the food to be fortified. The cost of fortification, the nutrient bioavailability in the fortified food, the shelf life of the fortified food and its storage conditions are goals to be reached. It is also important to select the most adequate level of fortification, and to promote the development of adequate country legislation to ensure continuity of the fortification programs (23-25).

Several iron salts have been tested such as ferrous sulfate, fumarate, gluconate, and lactate. In Guatemala and in Egypt, NaFeEDTA was tested in the fortification of sugar and wheat flour (26,27). Bovine hemoglobin concentrate, isolated from blood obtained in slaughter houses has been used for the fortification of biscuits, but it is uncertain if the product is completely free from microbiological and viral contaminations Hem iron is known to be good source of iron (28,29), but its isolation from animal blood may pose large problems to comply with the need of control of biological contamination of the fortified product. Most of the studies with hem have been carried out in Chile where hem iron bioavailability in milk, biscuits and extruded cereals has been investigated (29-31).

In Brazil, fortified cookies containing 3% bovine hemoglobin were given to children 2- 4 years of age attending day care nurseries in the community of Piaui. The children were fed 5 cookies (8,3 mg of iron) per day, which resulted in a hemoglobin increase of about 2 grams, from 11 to 13,2 g/dL. The results of the trial show the effectiveness of hem in the prevention of iron deficiency anemia (32-34).

The development and availability in the market of an iron bis-glycinate chelate in which, an atom of iron is bonded to two molecules of glycine by means of stable coordinated covalent bonds forming two heterocyclic rings, offered greater fortification possibilities due to the high bioavailability of the chelate, with the added advantage that this compound does not provoke organoleptic changes in the fortified food (19,20).

In a study designed to evaluate the bioavailability of the iron amino acid chelated in whole milk, the authors observed that the iron absorption from 3 mg Fe/L was 2 to 2,5 times higher than the observed absorption from a similar milk fortified with ferrous sulfate (35,36). The results indicate that even in the presence of the common inhibitors inorganic of iron absorption present in milk (casein, calcium, serum proteins and phosphates) the absorption of the amino chelate was not hindered (36).

According to Olivares (35), in milk, the bioavailability of the iron bis-glycinate chelate alone is similar to that obtained with ferrous sulfate plus ascorbic acid (33,35). The organoleptic characteristics of milk fortified with the iron amino acid chelated remained unchanged (36).

Some additional studies of milk fortified with iron bis-glycinate chelate have been carried out in Brazil.The São Paulo's Department of Health conducted a six-month study with 2 year old children who were given a milk fortified with 9 mg of iron from the amino acid chelate and 65 mg of ascorbic acid per 100 g of powdered milk (3 mg of iron and 13.6 mg of ascorbic acid per 250 ml of milk). The results demonstrate the effectiveness of milk fortified with the amino acid chelate in the prevention of iron deficiency anemia (21).

In 1995, in a study using *Petit-Suisse* cheese fortified with iron bis-glycinate chelate at a level of 2 mg of iron in 90 g of cheese per day, it was found that after 3 months of fortified cheese consumption, there was a significant increase in plasma ferritin levels from 15.69 to 24,68 µg/L (20).

In the district of Angatuba, Sao Paulo, in a population trial in which milk fortified with 3 mg iron per liter from iron bis-glycinate chelate was administered to children for a period of one year, a marked decline in the prevalence of iron deficiency anemia, from 62.3% to 41.8% was observed in six months. At the end of the year of consumption of iron-fortified milk, the anemia prevalence had dropped to 26.4 (36).

In 1995, Fisberg, *et al*, used iron bis-glycinate chelate to fortify wheat flour used to bake bread and cookies to a final iron level of 2 mg Fe/50 g of bread or 2 mg Fe/5 g biscuit. Nearly 900 children from 4 to 6 years of age received the fortified bread for three months at which time they showed an average increase in hemoglobin of 0.745 g/dL. Other 400 children from 6 to 36 months of age, received 2 fortified cookies per day for three months, and at the end of the intervention they presented a hemoglobin increase of 0,720 g/dL. The authors concluded that the use in the school meals, of bread or biscuits produced with flour fortified with iron bis-glycinate chelate was a safe and effective way of controlling iron deficiency and iron deficiency anemia, and that the fortification did not alter the organoleptic characteristics of biscuits or bread (21).

The aim of the present study was to evaluate the effect of consumption of sweet rolls fortified with iron bis-glycinate chelate, on the nutritional iron condition of preschool children.

MATERIAL AND METHODS

The study was carried out with preschool children of low socioeconomic level attending two day nurseries of the São Paulo's City Council. Children were kept in these day nurseries from 7 AM to 5 PM from Monday to Friday and received 5 meals per day.

When the study was started, 92 children were attending the nurseries, but three found severely anemic were treated and discarded from the study. These three children had an initial mean hemoglobin level below 9 g /dL. Of the remaining 89 children, 12 to 72 months of age, 52% were females and 48% were males.

Informed written consent and authorization for the study was secured, and signed by either the parents or the legal guardians of all children. The study's protocol was approved by the Medical Ethics Committee of the Federal University of São Paulo.

The study was divided into two phases: preintervention and the intervention proper that lasted 6 months. During the preintervention phase, all children were subjected to clinical examinations carried out by a pediatrician in order to evaluate the clinical status of each child and establish the presence of any preexisting illnesses that could interfere with their normal growth process.

At the beginning of the intervention, complete hematology tests were obtained from each child. All anthropometric measurements were carried out by well-trained personnel. The same measurements were repeated at the end of the six-month period of intervention.

During the nutritional intervention period children received their regular diet plus a sweet roll of 25 g fortified with 2 mg of iron from the amino acid chelate twice daily for five days a week. The total daily iron intake of 4 mg corresponded to 40% of the RDA) (37).

Body weight, recorded in kilograms, was obtained using a portable electronic digital scale with a total capacity of 150 kg and a sensitivity of 100 g. Height measurements were taken using a vertical stadiometer graduated in centimeters. The weight and height data was analyzed using EPI-INFO / EPI-NUT 6,02 (C.D.C. Atlanta, GA, U.S.A.). The weight/height, height/age and weight/age ratios data was evaluated according to the "z" score curve using the World Health Organization (WHO) reference standards (38,39).

For the analysis of hemoglobin and ferritin, 6 ml of blood were collected by venous puncture. Three mL of whole blood was kept in test tubes containing EDTA. This sample was used for hemoglobin determinations. From the rest of the 6 mL sample serum was obtained for the determination of ferritin. Hemoglobin concentration was measured electronically (Cell-Dyn 3000) (40), and the ferritin concentration by standard radioimmune assay procedures.

Fortified flour for the baking of the sweet rolls was obtained from Betamix (J. Macedo Alimentos Ltda. Sao Paulo). Each sweet roll weighed 25 g and contained 2 mg of iron from bis-glycinate chelate (Albion Laboratories, Inc. Clearfield, Utah, U.S.A.). Sweet rolls were selected because all subjects were used to their consumption.

RESULTS AND DISCUSSION

Nutritional condition

After the six months of intervention, mean values for weight/age and height/age of the children had increased significantly. At the beginning of the intervention, weight/age showed an average "z" score of - 0,23 and at the end of the intervention had risen to - 0,07. At the beginning of the intervention, the mean height/age "z" score was - 0,40 and at the end - 0,17 (Table1).

Iron condition

At the beginning of the study 28% of the children had hemoglobin levels < 11.0 g/dL, after 6 months of intervention the prevalence had decreased to 9%. The mean hemoglobin level at the beginning of the study was 11.5 g/dL and at the end 12.6 g/dL. (Table 2, Figure 1).

TABLE 1
Effect of 6 months of consumption of sweet rolls fortified with iron from Ferrochel on anthropometric indexes

Z score	Weight/Height Basal	Weight/Height Post-TX	Height/Age Basal	Height/Age Post-TX	Weight/Age Basal	Weight/Age Post-TX
≤ -2	2(2%)	1(1%)	7(8%)	2(2%)	3(3%)	2(2%)
>-2≤-1	8(9%)	8(9%)	20(23%)	20(23%)	18(20%)	13(15%)
>-1≤1	68(77%)	68(77%)	54(60%)	56(63%)	58(65%)	62(70%)
>1	11(12%)	12(13%)	8(9%)	11(12%)	10(11%)	12(13%)
Total	89	89	89	89	89	89
Mean ± S.D.(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	
Calculated z	-1,15		-5,5*		-4,8*	

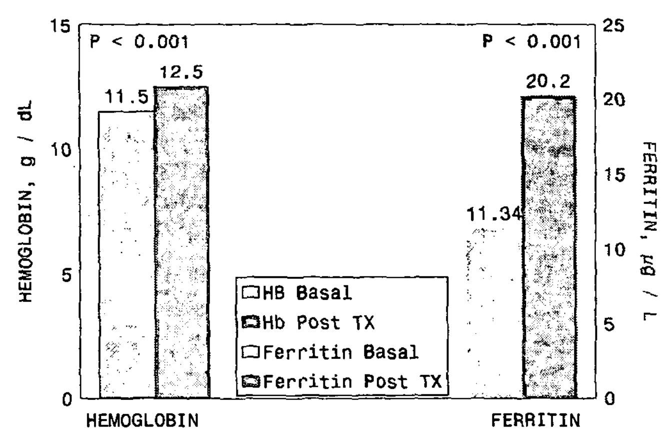
Wilcoxon critical z= 1,96; *P<0,001

TABLE 2
Effect of 6 months of consumption of sweet rolls fortified with iron from Ferrochel on the prevalence of anemia and levels of hemoglobin

Hemoglobin group	Basal N°. (%) g/dL ± s.d.	Hemoglobin Post TX N°. (%) g/dL ± s.d.	Mean change in Hb level g/dL
<11.00 g/dL	25(28%)	8(9%)	
	10,00±0,70	11,42±1,23	1,42
≥11.00 g/dL	64(72%)	81(91%)	
	12,07±16,70	13,03±1,03	0,96
Total	89(100%)	89(100%)	
Mean±S.D.	11,50±1,11	12,60±1,30	1,10

Wilcoxon test (B) x (TX), calculated z= 6,80. Critical z= 1.96, P <0,001. All Post-Tx changes are significant.

FIGURE 1



At the beginning of the study the mean hemoglobin level was 11,50 g/dL, the average gain after intervention was 1,10 g/dL. (Table 2, Figure 1). The prevalence of moderate anemia cases (Hb = 9 -10 g/dL) dropped from 12% at the beginning to 1% at the end, and the prevalence of children with hemoglobin levels 10-11 g/dL, decreased from 16 to 7%. In those children with basal hemoglobin levels below 11 g/dL the change after intervention was 1,42 g/dL, and in the group with basal levels greater than 11 g/dL the change after intervention was 0,91 g/dL (Table 2).

At the beginning of the intervention, of the 89 children studied, 55 (62%) had ferritin values of less than 10 µg/L and 34 (38%) had values greater or equal to 10 µg/L. The mean value for all children (89) was 11,34 µg/L. After six months of intervention this mean value had significantly increased to 20,2 µg/L.

The children that at the beginning of the study had depleted iron stores, with ferritin levels below 10 µg//L (55 children), after the six months intervention had a mean increase in ferritin level of 13,03 µg/L (2,36 to15,35 µg/L), see Table 3.

TABLE 3
Ferritin prevalence of low levels and change after 6 months of consumption of fortified sweet rolls

Ferritin level group	Ferritin Basal Prevalence (%) µg/L	Post TX Prevalence (%) µg/L	% change
<10.00 µg/L	255(62%)	22(25%)	
	2,32±2,29	15,35±11,57	661,6
≥10.00 µg/L	34(38%)	67(75%9)	
	25,93±16,70	28,04±10,30	8,1
Total	89(100%)	89(100%)	
	11,34±15,51	20,20±12,66	178,1

Wilcoxon test (B) x (TX), calculated z= -6,05. Critical = 1.96, P <0,001

It has previously been shown that iron absorption from the bis-glycinate chelate is regulated by the iron stores of the body (35). In line with this observation, the children with lower ferritin values that consumed the iron fortified sweet rolls, had the greater response in terms of increased serum ferritin levels.

CONCLUSION

After 6 months of consumption of sweet rolls fortified with 2 mg of iron from iron bis-glycinate chelate, we observed that:

1. The prevalence of anemia decreased significantly from 28 to 9%, and the prevalence of low iron stores decreased from 62 to 25%.
2. The mean hemoglobin levels of the children studied increased significantly (mean increase 1,10 g/dL). In anemic children, the increase was higher (1,42 g/dL).
3. The mean ferritin increase in the total group of children was 8,9 µg/L, and in children with depleted iron stores, the mean increase was 13,03 µg/L.
4 Anthropometrically, there was a significant increase in the "z" score for Weight/Age and Height/Age.
5. Sweet rolls fortified with 2 mg of iron from iron bisglycinate chelate are effective in the prevention and control of iron deficiency anemia at low cost and are, therefore, a good option for usage in programs of control of iron deficiency anemia.

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