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Iron bioavailability as a protective factor against anemia among children aged 12 to 16 months

Márcia Regina Vitolo,[1] Gisele Ane Bortolini[2]

Abstract

Objective: This study investigates the nutritional factors that determine the absence of anemia in infants from families with a low socioeconomic background submitted to a nutrition intervention program, as well as iron intake according to recommendations.

Methods: The study included 369 children from a cohort of inhabitants of São Leopoldo, state of Rio Grande do Sul, Brazil, who were randomized at birth into an intervention group and into a control group. The intervention group had nutritional guidance in the first year of life, with monthly follow-up home visits, whereas the control group was visited at 6 and 12 months, without nutritional intervention. At the end of the first year of life, a 24-hour recall was used. Anemia was diagnosed based on a hemoglobin level less than 11 g/dL. The children's diets were classified according to iron bioavailability.

Results: The prevalence of anemia amounted to 63.7% in this study. The proportion of children with adequate iron intake relative to the recommendations was statistically higher in the nonanemic group (26.8%) than in the anemic one (17.7%). Nonanemic children had a greater intake of iron ($p = 0.019$), vitamin C ($p = 0.001$), energy density at dinner ($p = 0.006$), iron density per 1,000 calories ($p = 0.045$); and 16.3% of them had a diet with high iron bioavailability ($p = 0.002$).

Conclusions: A diet with high iron bioavailability protects children from anemia and can be used as an intervention measure by basic health services and by the municipal departments of children's education.

J Pediatr (Rio J). 2007;83(1):33-8: Anemia, bioavailability, iron, child health.

Introduction

Iron stores at birth play a key role in determining the risk factors for childhood anemia, due to the low iron concentration in human milk.[1] The iron stores in exclusively breastfed infants, from birth to the sixth month of life, meet the infant's physiological requirements, thus eliminating the need for supplementation or introduction of solid foods.[2,3] This is due to the high iron bioavailability in human milk, with approximately 50% of iron uptake, which offsets its low concentration (0.5-1 mg of iron/liter). However, this bioavailability can decrease by 80% when other foods are ingested by the infant.[4] From the fourth to the sixth month, iron stores are gradually depleted, and feeding then plays a predominant role in meeting iron requirements. Iron intake should meet the requirements of this age group.[5] Thus, dietary habits in the first 2 years of life are important to prevent iron-deficiency anemia, since there is a high prevalence of such deficiency at this time.[6-9]

Despite that, few studies have confirmed this evidence by research on food intake.[10,11] In Brazil, in the last few years, studies have focused on investigating the effect of breastfeeding and artificial feeding on the prevalence of

1. Doutora. Programa de Pós-Graduação, Fundação Faculdade Federal de Ciências Médicas de Porto Alegre (FFFCMPA), Porto Alegre, RS, Brasil.
2. Mestranda, Programa de Pós-Graduação, FFFCMPA, Porto Alegre, RS, Brasil.

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anemia,[6-8,12-14] but the results were contradictory. There are only two studies in our setting that investigated the current food intake among small children.[15,16]

Therefore, the aim of the present study was to assess which dietary habits were associated with protection against iron-deficiency anemia in a population of children aged 12 to 16 months from families with a low socioeconomic background,[17] as well as the adequacy of iron intake to the new recommendations.[5]

Methods

Study participants were recruited at Hospital Centenário, the only existing hospital in São Leopoldo, Brazil, only at the divisions covered by the Brazilian Unified Health System (SUS). The sample size was based on the frequency of exclusive breastfeeding up to 4 months of 21.5% in the control group, and on a difference of 65% in the frequency of this practice between the groups. Other parameters used for this calculation included: a power of 80% and a 95% confidence interval, which determined that the sample should include 177 children in each group, totaling 354 children. Given that approximately 25% of the children could be lost to follow-up, 500 mother-child pairs were recruited so that the sample size could be attained. Newborn infants with birth weight ≥ 2,500 g and gestational age ≥ 37 weeks were considered eligible for the study. Exclusion criteria included: HIV-positive mothers, congenital malformation, infants referred to the intensive care unit and multiple pregnancies. Among eligible newborn infants, 90% of mothers agreed to participate after receiving information about the methodological differences between the intervention and control groups. Of every five mothers who agreed to participate in the study, two were randomly placed in the intervention group whereas the other three were assigned to the control group, and consecutively so, until the estimated sample size was obtained. The proportion of mother/child pairs in the control group was estimated based on the fact that the visit occurred only 6 months after the contact at the maternity ward, which may result in a larger loss to follow-up in this group. Thus, after randomization, 200 newborn infants were included in the intervention group and 300 in the control group. Home visitors (undergraduate Nutrition students) were trained to apply the nutritional intervention and to collect the data.

Intervention group – intervention consisted of nutritional guidance including the 10 steps towards the healthy nutrition of children younger than 2 years,[18] given to mothers during 10 home visits made on the first 10 days after delivery, monthly up to the sixth month and at 8, 10 and 12 months.

Control group – This group was visited at 6 and 12 months for the collection of anthropometric, nutritional, and sociodemographic data, and of information about the infant's health status. At 6 months, interviewers informed mothers about anthropometric results and told them to seek the nearest health service if any nutritional disorder was detected.

The present study assessed nutrition as a protective factor against anemia, regardless of the groups, considering the absence of effects of the intervention on the prevalence of anemia.[17]

The 24-hour diet recall, carried out by Nutrition students, recorded the child's food intake on the day before the last home visit, using rigorous criteria to describe the portions reported by mothers or surrogates, and the brand used, due to the high frequency of products fortified with micronutrients. For breastfed infants, the estimate of 448 mL/day was used for 12-month-olds.[19]

The NutWin (Nutritional Support Program of Universidade Federal de São Paulo - Unifesp) and food chemical composition tables were used to calculate nutritional values of the diets, in addition to information obtained from food industries about products not included in the tables. Of 369 children submitted to complete blood count, a 24-hour diet recall was obtained from 343, but 26 recalls were discarded due to the following reasons: incorrect or missing information (both the servings and amount ingested by the child should have been recorded) (seven), the child was sick (two), nonspecific home measures (13) and measures which mothers could not explain (four). The calories ingested at lunch and dinner were quantified separately, and milk-based meals were not considered if offered as a substitute to other foods.

The method developed by Monsen et al.[20,21] was used to assess the bioavailability of iron ingested by the children. This method is shown in Table 1.

Current recommendations suggest the use of the estimated average requirement (EAR), which corresponds to 3 mg/day for the age group analyzed. The value suggested by the recommended dietary allowance (RDA) (7 mg/day) was also used, which corresponds to the requirements of 97 to 98% of the whole population in the age group analyzed.[5] The mean, standard deviation and median of nutrients and of other consumption variables were calculated.

The complete blood count was performed at the Municipal Laboratory of São Leopoldo, using an automated cell counter (MDII). The cutoff points used to define anemia were hemoglobin level (Hb) < 11 g/dL and severe anemia Hb < 9.5 g/dL.

Table 1 - Dietary iron bioavailability

Low bioavailability	Intermediate bioavailability	High bioavailability
< 23 g of meat and < 75 mg of vitamin C	< 23 g of meat and > 75 mg of vitamin C	> 70 g of meat and > 25 mg of vitamin C
23-70 g of meat and < 25 mg of vitamin C	23-70 g of meat and > 25 mg of vitamin C	
	> 70 g of meat and < 25 mg of vitamin C	

Source: Monsen et al.[20]

The test for both groups was extended to the age of 16 months, due to rescheduling, as some mothers could not take their child when he/she turned 1 year old.

The study protocol was approved by the Research Ethics Committee of Universidade Federal do Rio Grande do Sul.

Student's *t* test and the nonparametric Mann-Whitney test were used for the association of nutritional factors with the absence of anemia, and the use of these tests was determined by Kolmogorov-Smirnov test; the chi-square test was used to assess independence or association between children with and without anemia. The relative risks (RR) and the respective 95% confidence intervals (IC95%) were calculated to quantify the effect of iron intake and its bioavailability on the occurrence of anemia. The null hypothesis was rejected at 5% on all tests.

Results

Of the 397 children who completed the cohort study, 369 were submitted to the complete blood count, and losses to follow-up (4.1%) occurred because some mothers refused to have their children's blood tested. The prevalence of anemia and of severe anemia among children amounted to 63.7 and 18.3%, respectively. The proportion of children with an iron intake higher than 7 mg in the nonanemic group corresponded to 26.8% and to 17.7% in the anemic group (RR = 0.72; 95%CI 0.53-0.98). An iron intake greater than or equal to 3 mg a day was not associated with Hb levels ≥ 11 g/dL (RR = 0.72; 95%CI 0.46-1.12), data not shown in the table. The average iron intake in nonanemic children was 5.71±2.82 mg/day, significantly higher than that of anemic children (5.03±2.40 mg/day). These values were higher than the EAR. The intake of meat, source of heme iron, among children aged 12 to 16 months was reported in 78.4% of questionnaires; however, the ingested amount was not sufficient.

As to the frequency of diets according to iron bioavailability and its association with the absence of anemia, there was a higher proportion (16.3%) of diets with high iron bioavailability in the nonanemic group, compared to the anemic one (10.5%). Children whose diet had intermediate or high iron bioavailability showed a reduction in the frequency of anemia by 22 and 28%, respectively, compared to children whose diet had a low iron bioavailability (Table 2).

The highest intake of iron (p = 0.01) and vitamin C (p = 0.00) was associated with absence of anemia in children. Nonanemic children had a significantly higher energy intake at dinner than anemic children (p = 0.00) (Table 3). The same analyses, not shown in the table, were carried out with children who did not have severe anemia (Hb ≥ 9.5 g/dL), and its absence was significantly associated with a larger intake of vitamin C (p = 0.04), heme iron (p = 0.04) and lower intake of calcium (p = 0.04). The average intake of cow's milk was statistically lower in children without severe anemia (523±315 mL) compared to those with severe anemia (648±387 mL) (p = 0.01). No association was observed between the absence of anemia and the following variables: nonheme iron, iron from fortified foods, calories at lunch, ingested amounts of meat and beans, separately.

Discussion

The high prevalence (63.7%) of anemia found in this study in full-term normal-weight newborns, from families attended to by the Unified Health System of São Leopoldo, highlights the importance of this problem among children aged 12 to 16 months.[6-9] The project known as "Implementation and Assessment of the Impact of the 10 Steps to Healthy Feeding: a Nutritional Guide for Children under Two Years" efficiently increased exclusive breastfeeding rates, reduced the occurrence of morbidities and tooth decay, but, on the other hand, was inefficient in the prevention of iron-deficiency anemia.[17]

In the present study, nonanemic children had a higher iron intake than anemic ones. A study[22] carried out in New Zealand, with a similar methodology to that of this study, revealed a median iron intake of 4.3 mg in 12-month-old children, a value that is similar to the one found in this study. In the present study, iron bioavailability was associated with iron nutritional status in children, suggesting that it is a useful indicator for assessment and intervention programs targeted at the prevention of iron-deficiency anemia. It is common knowledge that the amount of bioavailable iron is more important than to meet iron requirements, since this amount is related to factors that stimulate and inhibit its use in the same meal.[15,16,23] Lacerda & Cunha,[15] in a study with children aged 12 to 18 months in Rio de Janeiro, noted a low intake of total iron and of bioavailable iron, after applying a 24-hour diet recall. The average percentage of bioavailable iron relative to total iron corresponded to 7%, which characterizes a diet with low iron bioavailability.

Over 70% of children had eaten meat on the day before the interview, but the ingested amount was not sufficient. Studies demonstrated an association between low meat intake and anemia in children.[10,11] Nonanemic children ingested significantly more vitamin C than anemic ones. Thus, this study highlights the benefits of this micronutrient in the prevention of iron-deficiency anemia, especially in population groups in which meat intake is restricted due to its cost. Cook & Reddy[24] also showed the importance of vitamin C intake, which helps with the uptake of nonheme iron.

The prevention of severe anemia was observed among children with a lower intake of cow's milk and calcium, and higher calorie intake at dinner, suggesting that such eating practices should be included in nutritional guidelines for children in this age range. Other studies also found an association between anemia and the intake of cow's milk.[25,26]

Dietary questionnaires have limitations that must be taken into consideration. Although interviewers are trained for the task, there might be some biases in the collection of food intake data. Nutritional data reflect the current intake, and not the previous nutritional status, which may have caused iron deficiency. Moreover, the present study does

Table 2 - Association between dietary iron bioavailability and absence of anemia

	Children with hemoglobin levels < 11 g/dL		Children with hemoglobin levels ≥ 11 g/dL			
	n	**(%)**	**n**	**(%)**	**RR (95%CI)**	**p**
Dietary iron bioavailability						
Low	104	(47.3)	36	(29.3)	1	
Intermediate	93	(42.3)	67	(54.5)	0.78 (0.66-0.92)	0.00
High	23	(10.5)	20	(16.3)	0.72 (0.54-0.97)	
EAR						
< 3 mg	43	(19.5)	16	(13.0)	1	0.12
≥ 3 mg	177	(80.5)	107	(87.0)	0.72 (0.46-1.12)	
RDA						
< 7 mg	181	(82.3)	90	(73.2)	1	0.04
≥ 7 mg	39	(17.7)	33	(26.8)	0.72 (0.53-0.98)	

95%CI = 95% confidence interval; EAR = estimated average requirement; RDA = recommended dietary allowance; RR = relative risk.

Table 3 - Association between nutritional variables obtained from the 24-hour diet recall and absence of anemia among children aged 12 to 16 months

	Children with hemoglobin levels < 11 g/dL				Children with hemoglobin levels ≥ 11 g/dL				
	(n)	Median	Mean	SD	(n)	Median	Media	SD	p
Iron*	(220)	4.71	5.03	2.40	(123)	5.24	5.71	2.82	0.01
Heme iron (mg)*	(167)	1.04	1.34	1.00	(103)	1.26	1.46	1.14	0.34
Nonheme iron (mg)*	(220)	2.68	2.87	1.26	(123)	2.73	2.82	1.18	0.68
Iron from fortified foods (mg)*	(123)	1.57	2.05	1.78	(85)	1.83	2.47	2.12	0.13
Vitamin C (mg)†	(220)	30.94	43.75	34.87	(123)	38.72	56.97	42.88	0.00
Calcium (mg)*	(220)	617.15	691.86	442.04	(123)	600.39	686.43	391.19	0.91
Milk volume (mL)*	(171)	520.00	556.96	345.67	(104)	552.5	531.25	312.56	0.52
EV provided by milk*	(171)	319.49	336.91	210.99	(104)	325.64	314.67	191.78	0.37
EV at lunch*	(220)	168.12	172.11	168.12	(120)	180.04	181.69	86.33	0.32
EV at dinner†	(189)	122.21	132.39	71.04	(110)	154.68	156.18	80.04	0.00
Meat (g)*	(166)	49.0	48.85	24.95	(102)	49.7	51.81	26.74	0.36
Beans (g)*	(120)	58.5	67.97	47.22	(54)	53.5	68.97	49.74	0.86

EV = energetic value; SD = standard deviation;.
* Student's *t* test, † Mann-Whitney test.

not allow distinguishing between children with low iron stores at birth and the peculiarities of their uptake mechanisms.

The World Health Organization[1] recommends the universal use of iron supplements in the dose of 2 mg/kg a day for all children aged 6 to 23 months living in countries where the prevalence of anemia is ≥ 40%. However, food fortification is accepted as the best way to tackle specific nutrient deficiencies because of its high effectiveness,[27,28] since drug supplementation has a poor treatment adherence.[29]

Therefore, food composition, rather than the total amount of foods, is the most important element in the prevention of iron-deficiency anemia. An effort should be focused on warranting the offer of foods and preparations that provide high iron bioavailability. A daily meat intake greater than 70 g combined with the intake of vitamin C in amounts greater than 25 mg a day is a dietary practice that is associated with the absence of anemia among children with a low socioeconomic background and should therefore be implemented by the municipal departments of children's education and by the basic health system.

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Correspondence:
Márcia Regina Vitolo
Rua Sarmento Leite, 245,
Departamento de Saúde Coletiva, Sala 414
CEP 90050-170 – Porto Alegre, RS – Brazil
E-mail: marciavitolo@hotmail.com