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Greater effectiveness of daily iron supplementation scheme in infants

ABSTRACT

OBJECTIVE: To assess the effectiveness of weekly and daily schemes of preventive supplementation with supplementary iron to prevent iron deficiency anemia in non-anemic infants.

METHODS: A prospective population study with a quantitative approach and preventive intervention was performed in the city of Viçosa, Southeastern Brazil, in 2007-8. A total of 103 non-anemic children, aged between six and 18 months of age, were selected, corresponding to 20.2% of the children registered with and cared for by *Equipes de Saúde da Família* (Family Health Teams). Children were divided into two supplementation groups: daily dosage recommended by the *Sociedade Brasileira de Pediatria* (Brazilian Society of Pediatrics) (group 1, n=34) and weekly dosage recommended by the Brazilian Ministry of Health (group 2, n=69). Assessments were made in the beginning of the study and after six months, with hemoglobin dosage (portable ß-Hemoglobin-meter) and anthropometric and dietary assessments being performed and socioeconomic questionnaire applied. Impact indicators used were prevalence of anemia, hemoglobin variation, adherence to and side effects of supplements.

RESULTS: Groups were homogeneous in terms of socioeconomic, biological and before-intervention health variables. After six months of supplementation, higher means of hemoglobin were found in group 1 than in group 2 (11.66; SD=1.25 and 10.95; SD=1.41, respectively, p=0.015); in addition to lower prevalences of anemia (20.6% and 43.5%, respectively, p=0.04). Only "supplementation time" influenced severe anemia (p=0.009). Statistically significant differences were not found for the "adherence to supplementation" and "side effects" variables.

CONCLUSIONS: The daily dosage recommended by the *Sociedade Brasileira de Pediatria* was found to be more effective to prevent anemia in infants, when compared to the dosage used by the Ministry of Health. The weekly dosage recommended by the Brazilian government program needs to be reviewed to increase the effectiveness of prevention of anemia in infants cared for in public health services.

DESCRIPTORS: Iron, Dietary, administration & dosage. Ferrous Compounds. Anemia, Iron-Deficiency, prevention & control. Infant Nutrition. Child Health (Public Health). Intervention Studies.

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INTRODUCTION

Iron-deficiency anemia is a worldwide public health problem, affecting both developed and developing countries, with serious consequences to human health and the socioeconomic development of countries.[21] Although anemia occurs in all age groups, children aged between six and 24 months are those most vulnerable to this deficiency, due to their higher requirements of iron for growth.[9]

In view of this, official organizations[19] recommend that measures be implemented to prevent this nutritional deficiency in countries with a prevalence of anemia higher than 40%. Among the basic actions to prevent anemia, the following stand out: control of parasite infections; sanitary education associated with measures to increase iron intake, including promotion of maternal breastfeeding; food fortification; and drug supplementation.[13]

The use of supplementary iron has the advantage of bringing fast changes in the nutritional status of iron, in addition to its being a strategy that can be specifically directed towards higher-risk population groups.[14] Based on this fact, in Brazil, preventive supplementation for infants is usually adopted in the *Unidades Básicas de Saúde* (UBS - Basic Health Units). Traditionally, the recommendation from the American Academy of Pediatrics[5] and the *Sociedade Brasileira de Pediatria*[a] (SBP - Brazilian Society of Pediatrics) is used, providing ferrous sulfate in a dosage of 1mg of iron/kg/day for infants born full-term and with adequate weight, between six and 24 months of age. However, from 2005 on, the Brazilian Ministry of Health has followed the *Programa Nacional de Suplementação de Ferro* (PNSF - Brazilian Iron Supplementation Program) as a preventive iron supplementation strategy to control anemia in Brazil, recommending a weekly supplementation with ferrous sulfate syrup (25mg of iron) for infants aged between six and 18 months.[b]

Although there are different schemes and recommendations of preventive supplementation with iron salts during childhood, there is no consensus on the best strategy to be adopted yet.[7,8,12,17] In this way, the objective of the present study was to assess the impact of iron supplementation schemes to prevent iron-deficiency anemia in non-anemic infants, comparing the effectiveness of a weekly prophylactic dosage of iron (25mg of iron) with that of a daily dosage (1mg/kg/day).

METHODS

A prospective population study with a quantitative approach and preventive intervention of anemia for six months was performed in the city of Viçosa, located in the *Zona da Mata,* Southeastern Brazil. The population of this city was estimated to be 76,081 inhabitants in 2007.[c]

The process of implementation of the *Programa de Saúde da Família* (PSF - Family Health Program) began in 1997; subsequently, in 2007, there were 13 *Equipes de Saúde da Família* (ESF - Family Health Teams), who provided coverage to about 56% of the population living in the city. All ESFs were complete, including doctors, nurses, nursing assistants and community health agents (CHA). In addition to these professionals, six teams included dentists, dental office assistants and nutritionists.[d]

Children aged between six and 18 months, cared for by the city ESFs, were assessed between August 2007 and May 2008. Of all the 1,027 children in this age group and living in the city, 560 were cared for by the ESFs and the remaining ones were divided into: private institutions, health plans or visits to the city's health center.[d]

Selection of mothers and children occurred through an invitation sent to the homes by the CHAs and posters fixed in the UBSs. Assessments occurred in each UBS on previously booked days; children who missed their date of assessment were invited by the CHAs, through an active search, to go to the city's health center.

A total of 327 children participated, corresponding to 31.8% of all children in this age group and living in the city, and to 54.5% of all children cared for by the ESFs. Among these 327 children, there was a prevalence of anemia of 30.6% (n=100), of which 30 had severe anemia (hemoglobin [Hb]<9.5g/dL). The remaining children (n=227) were included in the study.

First, hemoglobin (Hb) measurement was performed by directly reading a portable Hemocue® photometer (Hemoglobinometer) from a blood sample obtained by puncturing the finger or heel. Anemic children (Hb <11g/dL)[19] were sent for medical care with the ESF to receive the therapeutic dosage of ferrous sulfate, thus being excluded from the study.

Non-anemic children (Hb ≥11g/dL) were placed into the two following groups: those who had already been receiving supplement based on the SBP's recommendations

[a] Sociedade Brasileira de Pediatria. Temas de nutrição em pediatria. Rio de Janeiro; 2001. (Edição Especial).
[b] Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Manual operacional do Programa Nacional de Suplementação de Ferro. Brasília; 2005 (Série A. Normas e Manuais Técnicos).
[c] Instituto Brasileiro de Geografia e Estatística. Dados populacionais 2007. Brasília; 2007[citado 2008 mar 04]. Disponível em: http://tabnet.datasus.gov.br/cgi/tabcgi.exe?ibge/cnv/popmg.def
[d] Secretaria Municipal de Saúde de Viçosa. Serviço de Vigilância Epidemiológica. Viçosa; 2007.

(1mg/kg/day) before this study and who continued to follow this scheme comprised group 1 (n=94); and those who had not received supplementation before the study were included in the group supplemented with PNSF's ferrous sulfate syrup (25mg of iron/week) and comprised group 2 (n=133). The distribution of children in both groups followed the requirements from the local health service. Possible influences caused by the higher preventive supplementation time for group 1 were taken into consideration in the statistical analysis and subsequently discussed.

It was possible to assess the impact of supplementation schemes in 103 (45.4%) children: 34 from group 1 and 69 from group 2. The reasons for non-inclusion of children in the analyses are shown in the Figure. The percentage of losses was higher in group 1 (63.8%) than in group 2 (48.1%). Losses from both groups did not differ from each other. In addition, by comparing losses with the children who completed the study, the only difference observed was mean age. These results minimize the possibility of final results having been influenced by bias from different losses and, in a way, guarantee that children who completed the study are representative of all the children initially assessed, except for mean age.

The absence of a control group occurred due to ethical aspects involved with children not being provided access to preventive supplementation, which is extremely important in this age group.

Information about families' socioeconomic conditions was obtained using a semi-structured questionnaire. Child weight and height were measured using a electronic pediatric scale, with a 15kg capacity and 10g graduation, and child anthropometer with a 1.5m extension and subdivision in millimeters. Measurements were taken according to Jellife's recommendations.[10]

Child dietary assessment was made using a food consumption frequency questionnaire (FCFQ), capable of characterizing the usual diet of individuals with a single application. FCFQ was selective for iron-rich foods (beef and/or pork, chicken, fish, liver, dark-green leafy vegetables and beans), and those that are stimulators (natural juices or fruits) and inhibitors (coffee, tea, chocolate powder and sodas) of iron absorption, being applied at the end of the study. Mothers also answered whether they were breastfeeding and, in case of a negative response, how long they had breastfed for.

Children were followed by ESF professionals, according to the UBS service routine. Six months after the initial assessment, a nutritional status reassessment, hemoglobin measurement and interview with the mothers, using a semi-structured questionnaire and including questions about adherence, side effects and interruption of the use of supplements, were performed.

Database was created using the EpiInfo software, version 6.04. Statistical analyses were performed with the SPSS software, version 15.0. Chi-square test or Fisher exact test were used to compare proportions when the value expected, in a certain space, was lower than five. Kolmogorov-Smirnov test was employed to observe adherence of numerical variables to the normal distribution. Student t test was used to compare two independent groups and Mann-Whitney test as its non-parametric correspondent. A 5% level of significance was considered.

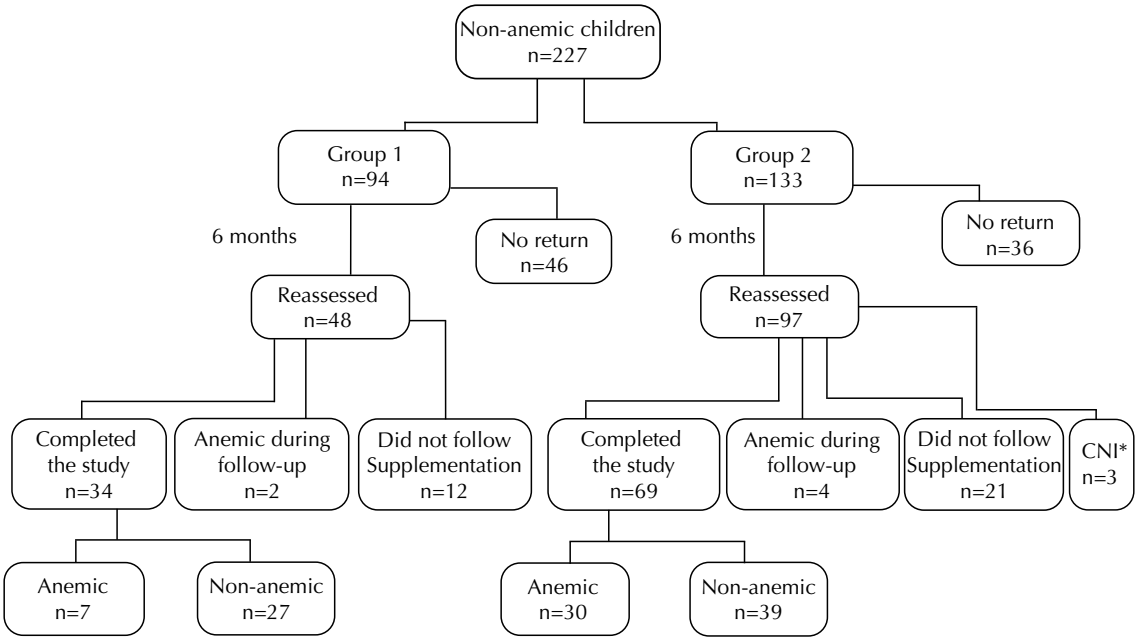
As children in group 2 had about six months of supplementation and those in group 1 had a longer time, supplementation time was included as a confounding variable in the statistical analyses of comparison between groups.

A linear regression model was developed for the Hg variation and Poisson regression models with a robust variation were adjusted for the anemia and severe anemia variables. Covariables that could influence the nutritional status of iron were initially included in the two processes. These were removed, one by one, until the final model included only those with a p value=0.05. Multivariate analysis was made in the public domain R software.

Infant nutritional status was assessed using the weight/age, weight/height, height/age and BMI/age indices, expressed as z-scores and using the World Health Organization (WHO) reference standard.[20]

Food consumption frequency was grouped into the three following categories to be analyzed: rare, one to three times/week and four to seven times/week. Rare, 15-day and monthly consumptions and non-consumption were included in the "rare" consumption category.[4] When the three frequencies of consumption were present in a certain group of foods, the statistical test was performed between the highest and lowest frequencies to compare supplementation groups.

Children who interrupted supplementation for a period of time higher than one month were excluded from the analyses. Adherence to supplementation was assessed for the remaining children using an indirect method that consisted of specific questions about use of ferrous sulfate, such as: difficulties, interruptions, acceptance and reports of the days and amount of supplement administered. In group 2, adherence was assessed according to the amount of syrup used during six months, based on information provided by mothers. Adherence was classified as high if the child had consumed more than 75% of the amount expected (>90ml), and low, if it had consumed less.[12] For the daily group, adherence was also self-reported. However, the number of days per week when the supplement was administered was reported. In this case, adherence was considered high



*CNI: Responsible adult could not inform

Figure. Diagram of the sample studied. Municipality of Viçosa, Southeastern Brazil, 2007-2008.

when this was above 75%, in terms of the number of days when the supplement was administered (>5 days), rather than the volume used. This occurred because the daily scheme includes a determined amount per kilogram of weight, resulting in variation of the volume used in children.

This research was approved by the Research Ethics Committee of the *Universidade Federal de Viçosa,* according to resolution 196 from the *Conselho Nacional de Saúde* (Brazilian Health Council).

RESULTS

Biological, food consumption and socioeconomic characteristics of children who completed the study were compared to subsequent losses, with a statistical difference for mean age, which was higher for losses (p=0.04) in both supplementation groups. Consequently, mean weight (p=0.048) and height were also higher (p=0.044), although a statistical difference between the nutritional status of these children could not be found (p>0.05) for any of the anthropometric indicators.

Both supplementation groups were similar to each other in terms of biological, food consumption and socioeconomic characteristics in the beginning of the study (Table 1). In general, families had a lower socioeconomic level, low maternal level of education, and low family and per capita income, although a great number of mothers lived with their partners and in an urban area.

By comparing groups 1 and 2 in terms of frequency of consumption of different foods, diet iron did not interfere differently in both groups (Table 2). Among the most bio-available sources of iron analyzed, high percentage of beef consumption and rare consumption of offal were observed. Among vegetable sources, high beans consumption stood out in the majority of children, although a much lower consumption of dark-green leafy vegetables was found. As regards foods that inhibit iron absorption, coffee appeared as the most frequently consumed food.

In the second assessment, a statistically significant difference was observed among the "mean Hb", "prevalence of anemia", "Hb variation" (final Hb subtracted from initial Hb) and "supplementation time" variables (Table 3). Higher prevalence of anemia was found in group 2, resulting in the risk of a child, supplemented by this scheme, having anemia being 2.11 times higher (95% CI: 1.04; 4.31) than that of children supplemented with a daily dosage (Table 4).

Multiple linear regression showed that lower Hb values were also found in group 2, with an average 0.7 g/dL of Hb less than group 1 (p=0.015; 95% CI: 0.1;1.3; standard-error=0.3).

A higher percentage of children (18.8%) in group 2 developed severe anemia, compared to group 1 (5.9%), although there was no statistically significant difference. This variable was only influenced by supplementation time, being less prevalent in children with longer supplementation time (Table 4).

Table 1. Biological, socioeconomic and health characteristics of infants and family members participating in the study per supplementation group, in the beginning of the study. Municipality of Viçosa, Southeastern Brazil, 2007-2008.

Variable	Group 1	Group 2	p
Male	52.9%	49.3%	0.726[a]
Mean age (SD)	11.79 months (1.25)	11.20 months (1.41)	0.453[b]
Mean weight (SD)	9.09 kg (1.61)	8.73 kg (1.76)	0.315[b]
Men height (SD)	72.91 cm (6.21)	72.09 cm (6.36)	0.539[b]
Mean weight/age (SD)	z-score -0.15 (1.019)	z-score -0.45 (1.290)	0.235[b]
Mean height/age (SD)	z-score -0.59 (1.480)	z-score -0.68 (1.500)	0.767[b]
Mean weight/height (SD)	z-score 0.32 (1.273)	z-score -0.06 (1.271)	0.155[b]
Mean BMI/age (SD)	z-score 0.26 (1.214)	z-score -0.06 (1.305)	0.230[b]
Mean capillary hemoglobin (SD)	12.44 g/dL (0.96)	12.36 g/dL (1.06)	0.695[b]
Mean birth weight (SD)	3145.47 g (398.39)	3118.55 g (501.46)	0.785[b]
Mean time of breastfeeding (SD)	8.50 months (4.329)	8.17 months (4.767)	0.737[b]
Mean maternal age (SD)	27.06 years (6.06)	27.65 years (7.09)	0.677[b]
Mother with a partner	82.4%	79.7%	0.749[a]
Urban residence	85.3%	78.3%	0.396[a]
Socioeconomic conditions			
Mean maternal level of education (percentiles 25-75)	8.00 years (4.0-11.0)	8.00 years (4.0-10.0)	0.542[c]
Mean family income (percentiles 25-75)	1.50 MW (1- 2.0)	1.00 MW (1.0 – 2.0)	0.101[c]
Mean per capita income (percentiles 25-75)	0.33 MW (0.25- 0.5)	0.33MW (0.25 – 0.4)	0.273[c]
Public water supply	94.1%	85.5%	0.200[a]
Public sewage system	94.1%	92.8%	0.796[a]
Owns a filter	94.1%	92.8%	0.796[a]
Owns a fridge	82.4%	89.9%	0.281[a]

[a] Chi-square test
[b] Student t test
[c] Mann-Whitney test
BMI: Body Mass Index
MW: minimum wage

As regards the "interruption of supplementation", "adherence to supplementation" and "side effects" variables, no significant differences were found between groups.

After the multivariate analysis, power between the response variables and covariables (administration of ferrous sulfate and supplementation time) was calculated. Power of the capillary Hb test was 0.74; that for anemia, 0.51; and that for severe anemia, 0.89. The low power of the anemia and Hb test is explained by the small sample size at the end of the study.

DISCUSSION

The low effectiveness achieved by preventive supplementary programs of anemia implemented in Brazil in the last years still poses a challenge to public health, in view of the high prevalences of the disease. The amount of elemental iron administered and the most adequate form of administration to prevent anemia in infants continue to be objects of discussion.

Although reductions in Hb levels were observed in both groups in the present study, the higher means of this parameter and lower prevalence of anemia were found in daily supplemented children.

In a study performed by Silva[a] with non-anemic infants, two groups following daily supplementation were compared to a group following a weekly dosage of 25 mg of iron. After four months of intervention, a higher incidence of anemia in the weekly group (27.6%) and lower levels of serum ferritin were found, although there was no statistically significant difference between

[a] Silva DG. Prevenção da anemia e da deficiência de ferro no segundo semestre de vida com diferentes suplementações de ferro [tese de doutorado]. São Paulo: Universidade Federal de São Paulo; 2007.

Table 2. Frequency of food consumption of source foods, inhibitors and facilitators of iron absorption in infants, according to supplementation group. Municipality of Viçosa, Southeastern Brazil, 2007-2008.

Food	Group	Food frequency			p[b]
		Rare[a]	1 to 3 times/week	4 to 7 times/week	
Meat	1	-	23.5% (8/34)	76.5% (26/34)	0.902
	2	-	24.6% (17/69)	75.4% (52/69)	
Offal	1	73.5% (25/34)	26.5% (9/34)	-	0.124
	2	56.0% (40/69)	42.0% (29/69)	-	
Beans	1	2.9% (1/34)	2.9% (1/34)	94.2% (32/34)	0.149[c]
	2	0.0% (0/69)	1.5% (1/69)	98.5% (68/69)	
Dark-green leafy vegetables	1	20.6% (7/34)	38.2% (13/34)	41.2% (14/34)	0.296[c]
	2	26.1% (18/69)	44.9% (31/69)	29.0% (20/69)	
Natural juices/citrus fruits	1	8.8% (3/34)	29.4% (10/34)	61.8% (21/34)	0.159[c]
	2	14.5% (10/69)	47.8% (33/69)	37.7% (26/69)	
Tea	1	100.0% (34/34)	0.0 (0/34)	-	0.217
	2	95.6% (66/69)	4.4% (3/69)	-	
Coffee	1	67.6% (23/34)	17.7% (6/34)	14.7% (5/34)	0.611[c]
	2	69.5% (48/69)	10.2% (7/69)	20.3% (14/69)	
Chocolate/chocolate powder	1	76.4% (26/34)	11.8% (4/34)	11.8% (4/34)	0.696[c]
	2	73.9% (51/69)	17.4% (12/69)	8.7% (6/69)	
Soda	1	76.5% (26/34)	23.5% (8/34)	0.0 (0/34)	0.188[c]
	2	63.8% (44/69)	31.9% (22/69)	4.3% (3/69)	

[a] Rare: 15-day period, monthly, rare, no consumption.
[b] Chi-square test
[c] Comparison between high-consumption group (4 to 7 times/week) and low-consumption group (rare).

mean Hb levels. Another study performed to assess PNSF impact, even though without an initial assessment of Hb in infants, showed the lack of effectiveness of the intermittent scheme proposed by the Brazilian Ministry of Health. Only the daily group showed an increase in mean Hb concentration, compared to the control group, in addition to a dosage-response effect of supplementation on the prevalence of anemia.[7]

In contrast, studies performed by Ferreira et al[8] and Monteiro et al[12] found good results with the use of weekly schemes of supplementation, with its use being recommended. However, these studies used higher dosages than those recommended by the PNSF. This finding reflects the possible insufficiency of the dosage proposed by the Ministry of Health's PNSF, rather than the inferiority of the weekly scheme, when compared to the daily scheme. In the present study, the low effectiveness of PNSF was observed in normal field conditions without supervision, once 43.5% of the children, initially non-anemic, developed the deficiency, even when supplemented.

Although no statistically significant difference was found, there was a high percentage of severe anemia in the weekly group, when compared to the daily one. Severe anemia has a clinical relevance, once this level of anemia contributes directly to mortality among women and children.[16] Thus, continuity of supplementation is key to prevent severe anemia.

In this sense, the preventive impact of supplementation is influenced by low adherence, in addition to the early interruption of use of the supplement. These aspects have been reported as obstacles to the success of supplementation with iron salts.[14] In this context, a weekly dosage was proposed as a strategy to improve adherence, due to both the lower frequency of administration and reduction in the side effects caused by the drug.[18]

The present study did not find statistically significant difference in the presence of side effects between the daily and weekly groups. Yurdakök et al[22] also observed similar percentages of occurrence of side effects in infants supplemented daily and weekly, indicating the absence of benefits of a scheme, when one is compared to the other.

In addition, the difference of assessment of adherence between supplementation groups may have contributed to the absence of statistical difference observed in relation to abandonment of supplementation and adherence. About 70% of the children reassessed showed good adherence to both forms of supplementation. Nonetheless, 33 children had interrupted the use of

Table 3. Anthropometric, socioeconomic and health characteristics of infants and family members participating in the study, according to supplementation group, after six months of intervention. Municipality of Viçosa, Southeastern Brazil, 2007-2008.

Variable	Group 1	Group 2	p
Mean age (SD)	17.82 months (3.93)	17.28 months (3.75)	0.493[a]
Mean weight (SD)	10.46 kg (1.72)	10.21kg (1.91)	0.516[a]
Mean height (SD)	80.44 cm (5.29)	79.63 cm (5.02)	0.452[a]
Mean weight/age (SD)	score-z -0.18 (1.167)	score-z -0.26 (1.291)	0.748[a]
Mean height/age (SD)	score-z -0.26 (1.214)	score-z -0.35 (1.186)	0.741[a]
Mean weight/height (SD)	score-z -0.15 (0.989)	score-z -0.14 (1.275)	0.993[a]
Mean BMI/age (SD)	score-z -0.09 (0.996)	score-z -0.13 (1.316)	0.869[a]
Socioeconomic conditions			
Mean family income (percentiles 25-75)	1.18 MW (1- 2.0)	1.00 MW (1.0 – 1.58)	0.233[b]
Mean *per capita* income (percentiles 25-75)	0.33 MW (0.25- 0.5)	0.26 MW (0.2 – 0.35)	0.231[b]
Supplementation			
Mean time of supplementation (percentiles 25-75)	7.00 months (6.67 -7)	6.00 months (6 - 6)	0.0001[b]
Hemoglobina capilar média (DP)	11.66 g/dL (1.249)	10.95 g/dL (1.414)	0.014[a]
Variação da hemoglobina (percentis 25-75)	-0.65 g/dL (-1.5 a 0.1)	-1.10 g/dL (-2.5 a -0.1)	0.048[b]
Prevalence of anemia	20.6%	43.5%	0.023[c]
Prevalence of severe anemia (Hb<9.5 g/dL)	5.9%	18.8%	0.079[c]
Good adherence to supplementation	76.5%	73.9%	0.778[c]
Interruption of supplementation	25.0%	21.6%	0.650[c]
Showed side effects	17.6%	18.8%	0.883[c]

[a] Student t test
[b] Mann-Whitney test
[c] Chi-square test
MW: minimum wage

supplementation and were excluded from the analyses; 82 children who had not been present during reassessment were not considered in the percentage of adherence. The low percentage of children who completed the study is in agreement with the study performed by Bortolini & Vitolo,[2] who reported limited adherence to the practice of supplementation, both in the daily (35.7%) and weekly groups (44.6%).

Moreover, the children assessed had a low socioeconomic level, exposing them to several risk factors such as anemia[a], thus comprising a priority vulnerable group. Silva et al[15] found that children from families with a per capita income of up to one minimum wage had an additional risk of 57% to have anemia.

One of the factors associated with income is the low consumption of iron-rich foods, which was not found in the present study. Although consumption of citrus fruits and dark-green leafy vegetables had been greater than that from other studies,[3,13] the increase in consumption of such foods must be promoted, once they are cheaper and can be grown in family gardens.

Although the present study mainly focused on preventive drug supplementation, the possibility of developing innovative strategies capable of reducing the prevalences of anemia in children, which are low cost and easy to be performed, such as fortifications of different foods or even the introduction of ferrous sulfate into the water of day care centers and homes.[1,6] Any measure to control anemia must be associated with actions that provide nutritional education and promote awareness of those involved.

Among the possible limitations of the present study is the difference in sample size between groups, once the distribution of children was performed respecting the local health service requirements, where all children who had not been previously supplemented should be included in the weekly supplementation. This fact also resulted in longer time of supplementation for the daily group, which could be considered a bias. However, this hypothesis was rejected by the results of statistical analyses made.

[a] Sociedade Brasileira de Pediatria. Temas de nutrição em pediatria. Rio de Janeiro; 2001. (Edição Especial).

Table 4. Poisson regression models with final robust variance for anemia and severe anemia in infants. Municipality of Viçosa, Southeastern Brazil, 2007-2008.

Model	Coefficient	Standard-error	p	PR	95% CI
I - Anemia (Constant)	-1.6	0.3	<0.001		
Group					
2 (Weekly)	0.7	0.4	0.040	2.11[a]	1.04;4.31
1 (Daily)				1[a]	
II - Severe anemia (Constant)	2.8	1.8	0.113		
Supplementation time	-0.8	0.3	0.009	0.40[b]	0.20;0.80

[a] Prevalence ratio without adjustment, once no potential confounding variable remained in the final regression model (variables tested: family income, per capita income, supplementation time, weight/height, public water supply, consumption of beans, citrus fruits and offal).
[b] Only supplementation time remained in the final model.

The absence of a control group was an important limitation in this study, once it restricted the possibility of more accurate comparative analyses being made. However, considering the great vulnerability of children, it would unethical to deny preventive supplementation.

Another limitation was the absence of assessment of more sensitive indicators of deficiency of iron such as serum ferritin and transferrin, using Hb as exclusive indicator of anemia. However, considering the fact that these analyses would involve a higher cost and imply a more invasive test, these parameters were not assessed. This did not compromise comparability of results, because the majority of studies found used only Hb as parameter to assess anemia.

The indirect method to assess adherence through interviews was selected because it is low cost and easily performed, although involving adherence overestimation bias as individuals could omit the way the treatment was performed from the interview. Nonetheless, this limitation is questionable for any type of survey, due to the interviewee's embarrassment, their desire to answer what would be appropriate, and the pressure, even if not intentional, of being asked questions.[11]

The possible limitations reported do not invalidate or reduce the clinical relevance of the superiority of the daily scheme, compared to the weekly one.

Thus, it can be concluded that the daily scheme or iron dosage of 1mg of iron/kg, recommended by the SBP, was a better indicator of impact on the mean Hb values and prevalence of anemia, when compared to the weekly dosage of 25mg of iron recommended by the PNSF, in addition to its not differing in terms of side effects and adherence to the supplement. As a result, the daily dosage recommended by the SBP was more effective to prevent anemia in infants aged between six and 18 months.

However, there was low adherence to supplementation in the two groups studied, represented by the high percentage of interruption of supplementation and by the proportion of incorrect drug use. A policy to promote awareness about the importance of preventive supplementation with iron salts is necessary both among mothers and health professionals. Regardless of the dosage and scheme selected, awareness is key to increase adherence to supplementation.

The weekly dosage recommended by the PNSF needs to be reassessed, in the sense of increasing its effectiveness to prevent anemia in infants cared for in public health services.

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