Eur J Nutr 39 : 263–269 (2000)

ORIGINAL CONTRIBUTION

V. M. Aguayo

School-administered weekly iron supplementation – Effect on the growth and hemoglobin status of non-anemic Bolivian school-age children

A randomized placebo-controlled trial

Summary *Background* Recent data suggest that daily iron supplementation of iron-replete children could impair their growth. If verified for weekly iron supplementation these results would markedly complicate targeting and implementing school-based weekly iron supplementation programs. *Aim of the study* To ascertain the effect of weekly iron supplementation on the growth and hemoglobin status of non-anemic school-age children. *Subjects and methods* 73 Bolivian non-anemic school-age children randomly assigned to the treatment group (n=37; receiving supplements containing $FeSO_4$ during 18 weeks) or the control group (n=36; receiving a placebo during the same period). Hemoglobin concentration and anthropometric measures were determined for each child at the beginning (T0) and the end (T18) of the study. *Results* The treatment group did not show any significant variation in hemoglobin concentration between T0 and T18 (–1.6±10.4 g/L; P=0.40) whereas the control group showed a significant decrease in hemoglobin concentration (–4.6±10.9 g/L; P=0.03). Anthropometric changes were not significantly different between the treatment and the control groups for weight, (1.63±1.11 kg vs 1.88±0.79 kg; P=0.30), height (2.35±0.94 cm vs 2.11±1.03 cm; P=0.34) or mid-upper arm circumference (0.29±0.57 cm vs 0.22±0.54 cm; P=0.64). *Conclusion* In our study, weekly iron supplementation of non-anemic school-age children had no negative effect on their growth while having a positive effect in preventing significant decreases in hemoglobin concentration. These results suggest that in regions where iron deficiency anemia (IDA) is prevalent, a simple and cost-effective way to control IDA in school-age children is to give weekly iron supplements to *all* children at school.

Key words Weekly iron supplementation – growth – hemoglobin – school-age children – Bolivia

Received: 5 June 2000
Accepted: 25 September 2000

V. M. Aguayo, Ph. D. (✉)
Senior Nutrition Policy Analyst
Academy for Educational Development (AED)
Social Development Division
Nutrition Programs
1825 Connecticut Avenue, NW.
20009 Washington DC

Introduction

Iron deficiency anemia is the most prevalent nutritional deficiency worldwide. It is a major public health problem with adverse consequences especially for women and children. Over 90 % of affected individuals live in developing countries [28]. Iron deficiency anemia in children is associated with decreased growth rates [4], impaired cognitive development [21, 31], reduced resistance to infections [26], increased fatigue [16], and poor school performance [20, 24].

In most countries, anemic children only receive iron supplements on the basis of diagnosed anemia. However, the continuing high prevalence of iron deficiency anemia among children in these countries shows that such an approach is not working. Poor health coverage of children at risk, especially in rural and suburban areas, and inadequate compliance, usually due to the side effects resulting from therapeutic doses of oral iron, are the main causes of the failure of iron supplementation programs [23]. Any finding that improves the distribution of iron supplements to children and their compliance with the treatment would therefore have important implications for the prevention and control of iron deficiency anemia in children.

In the last few years, several studies have demonstrated the biological efficacy of supervised intermittent iron supplementation in controlling mild to moderate anemia in

European Journal of Nutrition, Vol. 39, Number 6 (2000)

children. In these studies intermittent dosing of iron appears to improve children's hemoglobin levels equal to the standard daily regimen. A study in Indonesia [22] demonstrated that twice weekly iron supplementation (30 mg elemental iron/dose delivered as a syrup) had an effect similar to that of daily iron supplementation in children (2–5 yrs old) with low iron status. A study in China [14] found that a twice-weekly dose (6 mg elemental iron/kg body weight delivered as tablets) had no advantages over a weekly dose in iron-deficient children (3–6 yrs old) but did produce more side effects. An iron supplementation trial in Bolivia [1, 3] using lower doses of iron than the study in China (3–4 mg elemental iron/kg body weight delivered as tablets) showed that weekly administration of iron supplements corrected anemia as effectively as daily dosing in anemic school-age children (4–7 yrs old).

In Bolivia, the prevalence of iron deficiency anemia in school-age children ranges from 35 % to 60 % [2, 9]. In such a context, schools are an ideal setting for the implementation of weekly iron supplementation programs for the control of iron deficiency anemia in school-age children. The only feasible way to implement such programs would be to treat all children attending school because previous screening of hemoglobin levels to identify anemic children would increase the cost, time, technical skills, and logistical constraints needed to carry out the programs.

Iron supplementation of anemic children has been shown to improve their weight gain [5, 12, 13]. Moreover, recent research shows that daily and weekly iron supplementation have similar positive impact on weight gain in anemic school-age children. However, data from Indonesia suggest that daily iron supplementation of iron-replete children could result in a decreased weight gain in comparison to children given a placebo [11].

If verified for weekly doses of iron in school-age children, these results would bring into question the delivery of iron supplements to non-anemic children and markedly complicate targeting and implementing school-based weekly iron supplementation programs. To evaluate this concern, our study sought to ascertain the effect of weekly oral iron supplementation on the growth and hemoglobin status of non-anemic Bolivian school-age children living in a resource-poor community.

Subjects and methods

Subjects were Bolivian school-age children living in the outskirts of La Paz (4,000 m above sea level). The initial selection criterion was age within the range 6–11.9 years old and hemoglobin concentration > 144 g/L. Hemoglobin was determined in finger-prick blood samples with a Hemoglobin Photometer HemoCue (HemoCue AB; Angelholm, Sweden).

131 children attending school met the inclusion criteria for age. All 131 children were screened for anemia. 58 children (44.3 %) were anemic (hemoglobin concentration <=144 g/L) and 73 children (55.7 %) were non-anemic (hemoglobin concentration > 144 g/L). All anemic children received weekly iron supplements for 18 weeks. The 73 non-anemic children were randomly assigned to the treatment (n=37) or the control (n=36) group using a table with randomly assorted digits. During 18 weeks, children in the treatment group received tablets containing iron ($FeSO_4$) whereas children in the control group received a placebo similar in color and appearance to the iron supplement.

A teacher trained by the principal investigator was responsible for the delivery of the iron tablets in the classrooms. The teacher was provided with a list of the names of the children and the number and kind of pills (color-coded) each child should take every Wednesday. Children who were not present at school on Wednesday received the tablets on Thursday.

The iron dose was calculated to provide children with an average of 3 mg of elemental iron per kg of body weight. The supplement consisted of two types of tablets containing either 20 mg or 36 mg of elemental iron in form of $FeSO_4$. These tablets were used in combination to adjust the dose to the child's weight. For example, a child of 33 kg of body weight was given 1 pill containing 36 mg of elemental iron and three pills containing 20 mg of elemental iron (36+60=96) to come the closest possible to the 99 mg that would correspond to the child's weight (33x3=99).

Tablet administration began one hour after arrival at school in the morning. The teacher supervised the administration of tablets to the children with clean boiled water and made sure the children swallowed the supplements. The teacher recorded in a notebook compliance and side effects reported by children an/or their parents. Neither the teacher nor his assistant were aware of the composition of the tablets delivered to the children.

The design of the study enabled a randomized double-blind placebo-controlled trial with children in the treatment group receiving a weekly supplement of 3 mg of elemental iron/kg body initial weight (as recommended in the master protocol for WHO/UNU/UNICEF multi-country study of weekly iron supplementation) and children in the control group receiving a placebo.

At the beginning and the end (one week after supplementation ended) of the 18-week supplementation trial, hemoglobin concentration and anthropometric measures were determined for each child. Anthropometric assessment in both the treatment and the control group included measures of weight, height, and mid-upper arm circumference. Body weight was measured to the nearest 0.1 kg with an electronic weighing scale (SECA, Hamburg, Germany) while children were minimally clothed. Body height was expressed as the mean of three consecutive measurements to the nearest 0.1 cm with a WHO model height-measuring stadiometer while children were standing barefoot. Mid-upper arm circumference was measured to the nearest 0.1 cm with a linen tape. All measurements

were made by the same observer in accordance with Lohman et al. [15].

Tablet administration started two days after anemia screening and anthropometric assessment. The research proposal respected the International Guidelines for Ethical Review of Epidemiological Studies [6]. Informed consent was obtained from the parents of the children participating in the study. The protocol of the study was explained to and approved by the school board.

Statistical analysis

Z-scores of the indicators weight-for-age and height-for-age were calculated for all children with EPI-INFO 6.01 (Centers for Disease Control and Prevention, 1990) by using the National Center for Health Statistics (NCHS, 1977) data as a reference.

A one-sample Kolmogorov-Smirnov test was applied to establish that the hemoglobin concentration and anthropometric indicators were normally distributed. Student's 't' tests were used to test for differences in mean values between the treatment and the control group groups. Paired sample Student's tests were employed when examining changes within groups between the beginning and the end of the study. Chi-square analyses were conducted to test differences between groups in age and sex composition. Multiple linear regression analyses using the all variables method were performed to determine the most significant predictors of changes in hemoglobin concentration and anthropometric variables. A P value < 0.05 was considered significant in all statistical tests. All statistical analyses were computed using SPSS for Windows (SPSS Inc., Chicago, 1993)

Results

A complete set of data was obtained for 33 children in the treatment group (89.2 %) and for 31 children (86.1 %) in the control group. At baseline, anthropometric and hematological values of dropouts (4 in the treatment group and 5 in the control group) were similar to those of the children who completed the supplementation trial. In all nine cases, the reason for attrition was that the children's families moved to other settings.

In the final sample, mean age of children (Table 1) in the treatment group was not significantly different from that of the control group (110.9±23.8 months vs. 110.8±24.9 months respectively; P=0.99). Between group differences in age distribution (Table 2) were not significant either. The treatment group included 12 children 6–7.9 years old, 11 children 8–9.9 years old and 10 children 10–11.9 years old; the control group included 12, 8 and 11 children respectively in each age category (Chi-square test, P=0.80). Similarly, no significant differences were observed in sex distribution (Table 1) between the two groups. The treatment group included 16 boys and 17 girls whereas the control group included 18 boys and 13 girls (Chi-square test; P=0.44).

At baseline (T0), mean values of hemoglobin concentration, weight, height, mid-upper arm circumference, weight-for-age Z-score, and height-for-age Z-score in the two groups were not significantly different (Table 1).

Similarly at the end of the study (T18), no significant differences in hemoglobin concentration, weight, height, mid-upper arm circumference, weight-for-age Z-score, or height-for-age Z-score were observed between the treatment and the control groups (Table 1).

In the end of the study (T18), the number of children who had hemoglobin concentrations lower than or equal to 144 g/L was similar in both groups (5 children in the treat-

Table 1 Age, sex, hemoglobin concentration, and athropometric parameters of children at the beginning and at the end of the study[a]

	Control Group (n=31)	Treatment Group (n=33)
Beginning of the study (T0):		
Age (months)	110.9 ± 23.8	110.8 ± 24.9
Sex (boys:girls)	18:13	16:17
Hemoglobin (g/L)	157.4 ± 6.3	156.6 ± 6.0
Weight (kg)	25.1 ± 6.1	25.4 ± 5.7
Height (cm)	123.9 ± 10.2	125.1 ± 10.8
Mid-arm circumference (cm)	18.2 ± 1.9	18.0 ± 1.4
Weight-for-age (Z-score)	–1.09 ± 0.92	–0.96 ± 0.70
Height-for-age (Z-score)	–1.58 ± 1.04	–1.38 ± 0.89
End of the study (T18):		
Hemoglobin (g/L)	153.0 ± 9.0	155.0 ± 9.2
Weight (kg)	26.8 ± 6.6	27.0 ± 6.7
Height (cm)	126.1 ± 10.4	127.3 ± 10.8
Mid-arm circumference (cm)	18.3 ± 2.0	18.3 ± 1.6
Weight-for-age (Z-score)	–0.98 ± 0.92	–0.79 ± 0.56
Height-for-age (Z-score)	–1.59 ± 1.06	–1.35 ± 0.78

[a] Values are mean ± s. d. The treatment group was supplemented once weekly during 18 weeks with tablets containing 3 mg elemental iron/kg initial weight. The control group received a placebo similar in color and appearance. Differences between groups were tested by Student 't' test except for sex ratios (chi-square test).

Table 2 Children's age distribution at the beginning of the study

	Control Group (n=31)	Treatment Group (n=33)
6.0–7.9 yrs old	12	12
8.0–9.9 yrs old	8	11
10.0–11.9 yrs old	11	10

Chi-square test

ment group and 6 children in the control group). The number of children whose final hemoglobin concentration was more than 10 g/L higher than the initial concentration was similar in the treatment and the control groups (5 vs 6). The number of children whose final hemoglobin concentration was more than 10 g/L lower than the initial concentration was significantly higher in the control group than in the treatment group (12 vs 8) (Chi-square test, P=0.03).

The treatment group did not show any significant variation in hemoglobin concentration between T0 and T18 (–1.6±10.4 g/L; P=0.40), whereas the control group showed a significant decrease in hemoglobin concentration (–4.6±10.9 g/L; P=0.03) (Fig. 1).

Between T0 and T18, both groups showed significant increases in mean weight (P < 0.0001), height (P < 0.0001) and mid-arm circumference (P < 0.05). These changes were not significantly different between the treatment and the control groups for weight (1.63±1.11 kg vs 1.88±0.79 kg; P=0.30), height (2.35±0.94 cm vs 2.11±1.03 cm; P=0.34) or mid-upper arm circumference (0.29±0.57 cm vs 0.22? 0.54 cm; P=0.64).

Multiple linear regression analyses using the all vari-

Table 3 Variations in hemoglobin concentration and anthropometric parameters between the beginning and the end of the trial[a]

	Control Group (n=31)	Treatment Group (n=33)	P value[b]
Hemoglobin (g/L)[c]	–4.6 ± 10.9	–1.6 ± 10.4	0.26
Weight (kg)[d]	1.88 ± 0.79	1.63 ± 1.11	0.30
Height (cm)[d]	2.11 ± 1.03	2.35 ± 0.94	0.34
Mid-arm circumference (cm)[e]	0.22 ± 0.54	0.29 ± 0.57	0.64

[a] Values are mean ± s. d. The treatment group was supplemented once weekly during 18 weeks with tablets containing 3 mg elemental iron/kg initial weight. The control group received a placebo similar in color and appearance.
[b] P; difference between groups. Student 't' test.
[c] Within group variation in hemoglobin concentration in the treatment group was not significant (P=0.40) but reached statistical significance in the control group (P=0.03).
[d] Within group variation in weight and height was statistically significant (P < 0.0001) in both the treatment and the control group.
[e] Within group variation in mid-arm circumference was statistically significant (P < 0.05) in both the treatment and the control group.

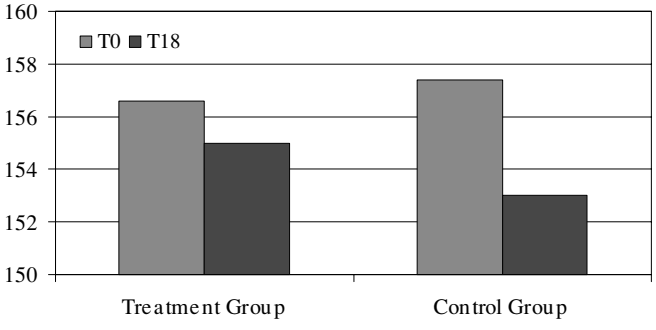

Fig. 1 Variation in hemoglobin concentration (g/L) between the beginning (T0) and the end (T18) of the study. Within group variation in hemoglobin concentration in the treatment group (–1.6±10.4 g/l) was not significant (P=0.40) but reached statistical significance (–4.6±10.9 g/l) in the control group (P=0.03). Paired Student t-test.

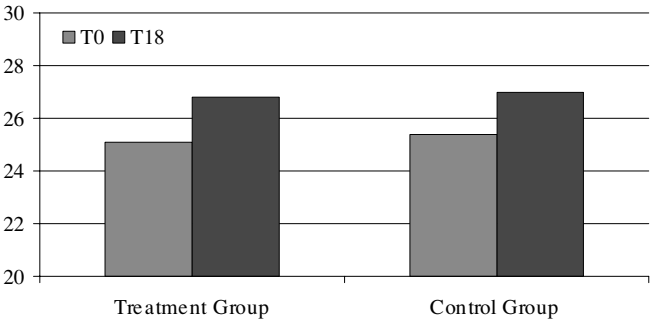

Fig. 2 Variation in weight (kg) between the beginning (T0) and the end (T18) of the study. Within group variation in weight was statistically significant (P<0.001) in both the treatment (1.63±1.11 kg) and the control group (1.88±0.79). Paired Student t-test.

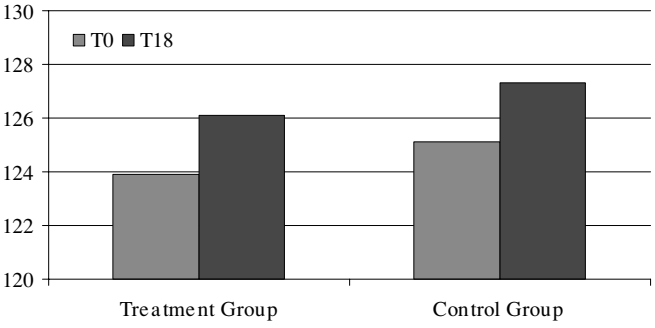

Fig. 3 Variation in height (cm) between the beginning (T0) and the end (T18) of the study. Within group variation in height was statistically sifnificant (P<0.001) in both the treatment (2.35±0.94 cm) and the control group (2.11±1.03 cm). Paired Student t-test.

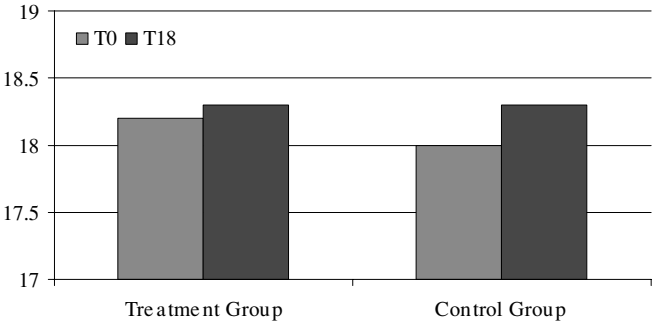

Fig. 4 Variation in mid-arm circumference (cm) between the beginning (T0) and the end (T18) of the study. Within group variation in mid-arm circumference was statistically significant (P<0.05) in both the treatment (0.29±0.57 cm) and the control group (0.22±0.54 cm). Paired Student t-test.

ables method showed that the only two significant predictors of weight gain over the supplementation period were the age and the initial weight. Similarly, the only two significant predictors of height gain over the supplementation period were the age and the initial height. Initial mean weight and height in the two groups were not significantly different. Nevertheless, despite randomization the proportion of underweight children (weight-for-age < –2 SD) in the control group was significantly higher than in the treatment group (0.30 vs 0.19; Chi-square test, p=0.04), possibly indicating a greater potential for weight gain in the control group. After correcting for the initial age and weight by including them in the analysis of variance, the between group differences in treatment effect for weight gain (tested by the interaction between treatment effect and supplement type) were not statistically significant.

Only one girl in the treatment group reported undesirable side effects (nausea) by the end of the study, but she completed the 18-week treatment. All children who completed the study in either group received at least 17 doses.

Discussion

For the purpose of screening, anemia was defined in our study by a hemoglobin concentration lower than or equal to 144 g/L. This cut-off value has been previously recommended for the definition of anemia in school-age children living at 4000 m above the sea level [1, 3]. The prevalence of anemia in the base population of our study was 44.3 %. This figure is consistent with previous estimates pointing out high prevalences of anemia among Bolivian school-age children living at high altitude [2, 9].

An increase in hemoglobin concentration greater than 10 g/L in response to iron supplementation is usually considered as evidence of initial iron deficiency anemia in children [8]. In our study, the number of children in the treatment group who responded to the weekly iron supplementation by an increase in hemoglobin concentration greater than 10 g/L was low (n=5). This number was not significantly different than the number of children in the control group who showed the same response at the end of the study (n=6). Therefore, children classified as non-anemic were truly non-anemic.

The duration of our study (18 weeks) and the dose of elemental iron given to children (3 mg/kg initial weight) were the same as in the study by Idjradinata et al. [11]. However, the supplementation scheme (one weekly dose) and the age group (64 school-age children) in our study were different from the supplementation scheme (daily dose) and the age group (47 preschool children) in the study by Idjradinata et al. in Indonesia.

Idjradinata et al. found that after four months of daily supplementation, the group receiving a placebo showed greater weight gain than the iron-supplemented group. However, at baseline the control group was slightly lighter for age than the iron-supplemented group, possibly indicating a greater potential for weight gain. Moreover, borderline between-group differences in morbidity could also explain differences in growth potential. The between-group difference in weight gain was not statistically significant. However, with repeated-measures analysis, there was a significant interaction between treatment group and weight gain. These controversial findings could therefore be the result of a peculiar data subset from a larger study designed to test the developmental consequences of iron deficiency anemia in childhood [10].

In our study, the treatment group did not show any significant variation in hemoglobin concentration after 18 weeks of weekly iron supplementation. The control group instead showed a significant decrease in hemoglobin concentration between the beginning and the end of the study.

No significant between-group difference was found with respect to weight, height, mid-upper arm circumference, weight-for-age Z-score, or height-for-age Z-score either in the beginning or the end of the study. Both the treatment and the control group showed significant increases in anthropometric measures with respect to the initial ones. These augmentations were not significantly different between groups. The main predictors of weight and height gain were the age and the initial weight or height of children, respectively. After correction for age and initial weight or height, the between-group differences in weight, height, weight gain and height gain remained not statistically significant.

The International Nutritional Anemia Consultative Group (INACG), WHO, and UNICEF recommend that a daily dose of 2 mg iron/kg weight be given to children 6–24 months of age for the prevention of anemia [25]. The dose given to children in the Indonesian study was significantly higher (3 mg/kg body weight/day). This could have translated into lower absorption rates of nutrients in the supplemented children due to the intestinal blocking by the preceding dose (-s) of iron and result in the observed adverse effect on weigh gain in iron-replete children. A weekly supplementation schedule would allow for a longer period for the absorption of iron, and avoid intestinal overload, and prevent any adverse effect on weight gain.

In our study, weekly iron supplementation of non-anemic Bolivian school-age children had no negative effect on their growth while having a positive effect in preventing significant decreases in hemoglobin concentration.

Program implications

In Bolivia, little progress has been accomplished over the last decade in controlling iron deficiency anemia in school-age children [9] despite the well-documented negative consequences of iron deficiency anemia on school performance, mental acuity, and concentration [27].

The control of iron deficiency anemia in school-age

children has mostly relied on programs that attempt to distribute therapeutic daily iron supplements to children through the primary health care system on the basis of diagnosed anemia. The effectiveness of such programs has been very weak likely because of the low coverage of the health care system in rural and periurban areas, the operational constraints of such programs, and the poor compliance associated with the daily regimen [30].

Recent school-based studies in Bolivia have shown that the administration of a weekly dose of iron to anemic school-age children is as efficacious as a daily schedule in controlling iron deficiency anemia [1, 3]. Therefore, supplementation programs for the control of iron deficiency anemia in school-age children could significantly improve their effectiveness through a school-based weekly supplementation approach. Such an approach could significantly increase coverage and reduce costs. It would also improve the compliance of the target group given that side effects of iron supplements are dose-related [29].

However, previous screening of hemoglobin levels to identify and target anemic children would significantly increase the cost, time, technical skills, and logistical constraints needed to carry out such school-based weekly supplementation programs.

In our study, weekly iron supplementation of non-anemic children showed no negative effect on their growth while preventing significant stresses in hemoglobin status. These results suggest that in regions like the Bolivian highlands (*Altiplano*) where iron deficiency anemia is prevalent, the simplest and most cost-effective way to prevent and control iron deficiency anemia in school-age children would be to give weekly iron supplements to all children at school.

Such a strategy would have positive effects for all beneficiaries. In the case of children who suffer from iron-deficiency anemia when they enroll in school, a weekly iron supplementation program would lead to the correction of iron deficiency anemia in a relatively short period of time [1, 3]. In the case of children who do not suffer from iron-deficiency anemia when they enroll in school, weekly iron supplementation would protect them, as seen in our study, from significant stresses in hemoglobin status related to seasonal variations in iron intake and/or iron utilization, growth, and infections.

In both cases, a long-term weekly iron-supplementation program would allow for the progressive accumulation of adequate iron reserves, which would protect children from iron deficiency and anemia, improve their school performance, strengthen their immunity, and prevent anemia during adolescence [27]. This is particularly important in countries like Bolivia where many girls marry and begin childbearing shortly after they finish school [7].

References

1. Aguayo VM (1996) Anemie nutritionnelle par carence en fer chez l'enfant: strategies d'intervention. Implications pour le developpement desecoliers Boliviens vivant en haute altitude. Ph. D. Dissertation. INA-PG/Pierre-et-Marie Curie. University of Paris
2. Berger J, San Miguel JL, Aguayo V, Tellez W, Lujan C, Traissac P. (1994) Definicion de la anemia en altitud. Efecto de una suplementacion con hierro y folato sobre los parametros hematologicos y evaluacion del estado nutricional de los nihos del Altiplano boliviano. Informe para la OMS de un estudio ORSTOM-IBBA
3. Berger J, Aguayo VM, Tellez W, Lujan C, Traissac P, San Miguel JL (1997) Weekly iron supplementation is as effective as 5 day per week iron supplementation in Bolivian school children living at high altitude. Eur J Clin Nutr 51 (6): 381–386
4. Bhatia D, Seshadri S (1993) Growth performance in anemia and following iron supplementation. Indian Pediatrics 30: 195–200
5. Chwang L, Soemantri AG, Pollitt E (1988) Iron supplementation and physical growth of rural Indonesian children. Am J Clin Nutr 496–501
6. CIOMS – Council for International Organization of Medical Sciences. (1991) International guidelines for ethical review of epidemiological studies. Geneva
7. DHS – Encuesta Nacional de Demografía y Salud (1998) INE/ENDSA, La Paz, Bolivia and Macro International, Calverton (MD), USA
8. Estrella R, Hercberg S, Maggy G, Larreategui J, Yépez R (1987) Evaluation of iron-deficiency anemia by an iron supplementation trial in children living at 2800 m altitude. Clin Chim Acta 164–168
9. Fernández EA (1996) Prevalencia de anemias nutricionales en mujeres embarazadas y escolares en Bolivia. Ministerio de Desarrollo Humano. Secretaria Nacional de Salud de Bolivia
10. Idjradinata P, Pollitt E (1993) Reversal of developmental delays in iron-deficient anemic infants treated with iron. Lancet 341:1–4
11. Idjradinata P, Watkins WE, Pollitt E (1994) Adverse effect of iron supplementation on weight gain of iron-replete young children. Lancet 343: 1252–1254
12. Latham MC, Stephenson LS, Kinoti SN, Zaman MS, Jurz KM (1990) Improvements in growth following supplementation in young Kenyan school children. Nutr 6: 159–165
13. Lawless JW, Latham MC, Stephenson LS, Kinoti SN, Pertet AM (1994) Iron supplementation improves appetite and growth in anemic Kenyan primary school children. J Nutr 124: 645–654
14. Liu XN, Kang J, Zhao L, Viteri FE (1995) Intermittent iron supplementation in Chinese preschool children is efficient and safe. Food and Nutrition Bull 16: 139–145
15. Lohman G, Roche AF, Martorell R (1988) Anthropometric standardization reference manual. Human Kinetics Books, Champaign. Illinois
16. Lozoff B, Klein NK, Prabucki KM (1986) Iron-deficient anemic infants at play. Journal of Developmental and Behavioral Pediatrics 7: 152–158
17. National Center for Health Statistics (1977) NCHS growth curves for children, birth–18 years. United States Department of Health, Education, and Welfare, Washington D.C, (PHS 78–1650)
18. Palupi L, Schultink W, Achadi E, Gross R (1997) Effective community intervention to improve hemoglobin status of preschoolers receiving once-weekly iron supplementation. Am J Clin Nutr 65 (4): 1057–1961
19. Norusis MJ. SPSS for Windows. (1993) Advanced statistics, release 6.0 Chicago. SPSS Inc

20. Pollitt E (1990) Iron deficiency and anemia. In: Pollitt E. Malnutrition and Infection in the Classroom. UNESCO
21. Pollitt E (1991) Effects of a diet deficient in iron on the growth and development of preschool and school-age children. Food and Nutrition Bulletin 2: 110–118
22. Schultink W, Gross R, Gliwitzki M, Karjadi D, Matulessi P (1995) Effect of daily vs twice weekly iron supplementation in Indonesian preschool children with low iron status. Am J Clin Nutr 61: 111–115
23. Schultink W, Gross R (1996) Iron deficiency alleviation in developing countries. Nutr Res Rev 9: 281–293
24. Soemantri AG, Pollitt E, Kim I (1986) Iron deficiency anemia and educational achievement. Am J Clin Nutr 42:1221–8
25. Stoltzfus RJ, Dreyfuss ML (1998). Guidelines for the use of iron supplements to prevent and treat iron deficiency anemia. ILSI Press. International Life Sciences Institute. Washington DC
26. Thibault H, Galan P, Setz F (1993) The immune response in iron-deficient young children: effect of iron supplementation on cell-mediated immunity. Eur J Pediatr 152: 120–124
27. UNICEF/UNU/WHO/MI (1998) Preventing iron deficiency in women and children. Technical consensus on key issues. New York. N. Y.
28. United Nations ACC/SCN (1997) Third report of the world nutrition situation. Geneva: ACC/SCN
29. Viteri FE, Ali F, Tujague J (1999) Long-term weekly iron supplementation improves and sustains non-pregnant women's iron status as well or better than currently recommended short-term daily supplementation. J Nutr 129 (11): 2013–2020
30. Viteri FE (1997) Iron supplementation for the control of iron deficiency in populations at risk. Nutr Rev 55 (6): 195–209
31. Walter T (1993) Impact of iron deficiency in cognition in infancy and childhood. Eur J Clin Nutr 47: 307–316
32. WHO/UNU/UNICEF (1993) Master Protocol. Population studies of the relative effectiveness of weekly and daily iron supplementation in pregnant women, adolescent girls and preschool age children. Geneva, November 18