Original Article

Effect of iron fortification of nursery complementary food on iron status of infants in the DPRKorea

HuiYong Rim MD, SuHuan Kim MD, ByongChel Sim MD, HaeYong Gang MD, HoYong Kim MD, YongRan Kim MD, RakChel Kim MD, MunHui Yang MD and SangPil Kim MD

Institute of Child Nutrition, Academy of Medical Sciences Saesalim Dong, Tongdaewon District, Pyongyang, DPR of Korea

The aim of this study was to determine the iron status of infants who consumed porridge cooked in water with added ferrous sulphate. A total of 234 infants, aged 6~12 months, were recruited from 36 nurseries in the Democratic Peoples Republic of Korea (DPRK North Korea) and randomly divided into iron (Fe) and placebo groups. At baseline, almost half the children had Hb<110 g/L and no significant differences between the two groups were found with regard to hemoglobin concentration and anemia prevalence. The Fe group received rice porridge fortified with 10 mg of iron (as ferrous sulfate) per day, added to the water in which the rice was cooked and the placebo group non-fortified cereal for 6 months. After which, the hemoglobin (Hb), serum ferritin (SF) and packed cell volume (PCV) were measured and it was found that the proportion of children with anemia (Hb<110 g/L) was lower (24.3% v 48.1% $p< 0.01$), the Hb levels (117.6 g/L v 109.8 g/L $p<0.001$) and serum ferritin were higher (40.7 v 26.8 mcg/L $p<0.001$); and iron deficiency anemia (Hb<110 g/L, SF<12 mcg/L) was lower in the Fe group (3% v 22% $p<0.001$) when compared to the placebo group. Ferrous sulphate, added to the water in which rice was cooked, lowered the prevalence of iron deficiency anemia of infants in the DPRK with no adverse reactions. This simple fortification would be suitable as a nationwide program in the DPRK and other countries with large infant nurseries.

Key Words: iron status, iron deficiency anemia (IDA), iron fortification, infant, nursery food

INTRODUCTION

The WHO estimates that more than 46% of children under the age of two years and 50% of pregnant women have iron deficiency anaemia worldwide.[1] The Multiple Indicator Cluster Survey (MICS) carried out in 1998 in the DPRKorea, revealed that 32% of children under 5 years, and 33% of women of reproductive age suffered from anemia.[2] Infants less than one year are at especial risk[3-7] but there have been few successful interventions.[8] About 80% of the children in DPRK aged 4 months – 4 years are enrolled in the government nursery system. The government provides most of the foods used in the nurseries; cooking is done in the nursery kitchen and the children are fed there. This system can be used to provide nutritional supplements and to monitor their effects. Rice is a staple food and ferrous sulphate added to the water used to boil the rice should be absorbed by the rice and provides a simple, safe and cost-effective way to increase iron intake. This project aims to determine the effects of such iron fortification of rice served in nurseries on the iron status of infants. The result of this research will serve as the basis to establish an intervention strategy for the prevention of IDA in DPRK.

MATERIALS AND METHODS

Study Design and Sampling

The project is a randomized, controlled, double blind study. Healthy infants at 6-12 months of age were recruited from 36 nurseries in 3 districts (Dongdaewon, Taedonggang and Sonkyo) of Pyongyang, DPRK. This area is situated in the east part of Pyongyang, is densely populated, and has a well-developed nursery-kindergarten network. All sub-districts in the area have similar geographic and socio-economic conditions and all nurseries have their food provided by the same nursery-kindergarten supply agency (NKSA). There is no ongoing iron intervention program for infants in the area.

Children with haemoglobin < 90g/L, low birth weight, chronic infection or congenital defect and twins were excluded after screening. The infants with severe anemia (Hb<90g/L) were brought to the doctor. Two hundred and fifty infants were screened, but using these criteria, 16 were excluded. The parents of the infants were given general information on the study and gave consent before the interview and initial blood collection. Ethical approval for the study was obtained from Academy of Medical Science and the Ministry of Public Health of the DPR Korea.

Corresponding Author: Rim HuiYong, nutrition epidemiology in the Institute of Child Nutrition, Academy of Medical Sciences Saesalim dong, Tongdaewon District, Pyongyang, DPR Korea.
Tel: 850-2-18111; Fax No fax is available
Email: med.intl@co.chesin.com
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Intervention

Soluble granules (coarse powder like table salt) of ferrous sulphate and a placebo were manufactured in Child Food Factory of Pyongyang, DPRK and packaged in amounts suitable for use by cooks in the nurseries.

The cooks dissolved the iron containing granules or placebo granules in the water in which the rice was cooked at the time of cooking. The granules were added so as to give 10 mg of elemental iron per child per day. Infants in the placebo group were fed with the same food with added placebo for the same period as the Fe group.

Infants were randomly assigned to the Fe group and placebo group. Infants in the Fe group were fed iron-fortified food twice a day, 6 days a week, for 6 months.

Data Collection and Management

During baseline data collection, the mothers were interviewed by trained researchers and information on the general characteristics of the children such as age, gender, birth weight, infant feeding practices, use of iron-supplements and history of illness, and also information about the mother e.g. occupation and education were obtained. The health card of the child was checked to ensure the accuracy of the information from the mothers. The nursery health worker recorded the morbidity of subjects every day throughout the study. Body weight and height were measured bi-monthly by well-trained researchers. Naked weight was measured using Seca baby scales (to the nearest 10g) and length was measured using a recumbent stadiometer (UNICEF). EpiInfo produced by the CDC (the Center for Disease Control and Prevention, U.S.A.) was used for the analysis of Z-score for weight-for-age, height-for-age-and weight-for-height.

Capillary blood samples for biochemical assay at baseline and end of the study were obtained by finger prick. At baseline, the hemoglobin concentration (Hb) was measured directly in the field by the field researcher using a portable hemoglobin photometer (Hemocue. Angelhelm. Sweden). At the end of the study, packed cell volume (PCV) was measured with the microhematocrit method and serum ferritin (SF) was analyzed by enzyme-linked immuno-solvent assay (ELISA) for quantitative determination of in vitro ferritin. Duplicate measures were done for quality control. The measurements were repeated when the duplicates differed by >10%. Children with illnesses and symptoms of current infection during the time of blood collection were rescheduled after two weeks.

Data analysis

Data were analyzed using SPSS software (Statistical Package for the Social Science, Windows version 10.0, SPSS, Inc, Chicago). The variables were presented as means + SD, geometric means (SF) and proportions. Skewed variables, e.g., serum ferritin, were log-transformed. The difference of means between groups was analyzed by independent t-test. Categorical data were analyzed by the Chi-square test. A p-value of 0.05 was considered statistically significant.

RESULTS

A total of 250 infants at 6~12 months of age from 36 nurseries were screened according to the entry criteria. Of those, 234 eligible infants were randomized to the iron-fortified group (117) and the control group (117). During the study, 23 infants (9.8% of all) dropped out from the study and in 24 infants we failed to measure a final blood specimen due to errors in handling the samples. Consequently, a total of 187 infants completed the final assessment including PCV and SF measurements. These profiles are shown in Figure 1.

Baseline characteristics of the two groups

General characteristics of the two groups are shown in

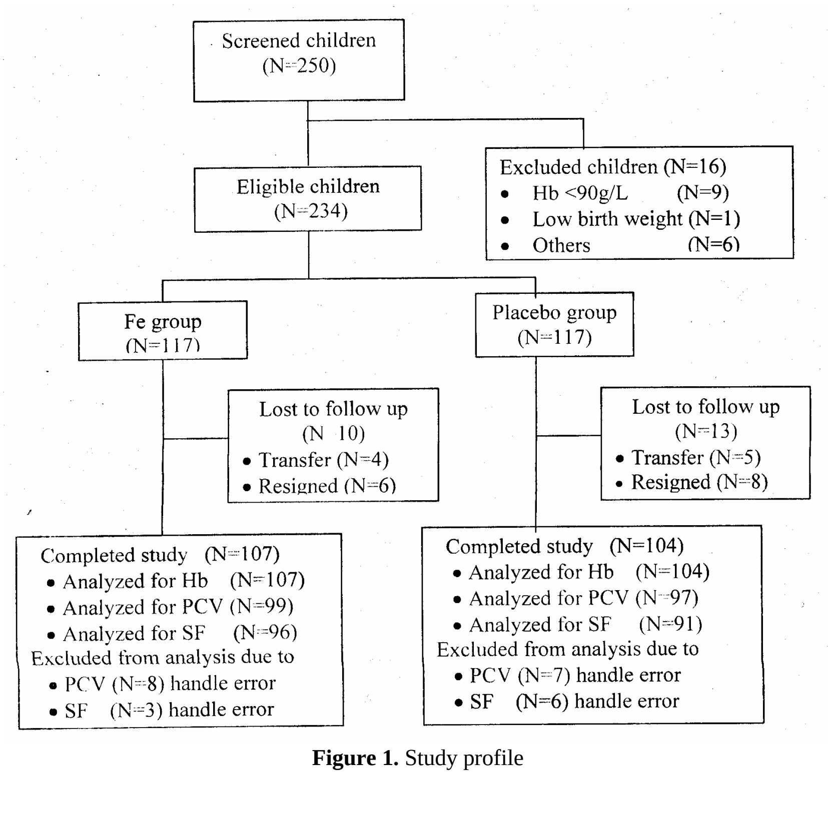

Figure 1. Study profile

Table 1. Comparison of baseline characteristics between the two groups

Variables	Fe group (n = 117)	Placebo group (n = 117)	*p*-value
Infant characteristics			
Boys (n (%))	61 (52)	58 (50)	0.794
Age (month)	9.55 ± 1.83†	9.41 ± 1.80	0.563
Gestation (weeks)	40.1 ± 0.9	40.1 ± 0.8	0.879
Birth weight (g)	3117 ± 326	3127 ±302	0.817
First child (n (%))	89 (76)	87 (74)	0.880
Exclusive breast feeding			
> 4month (n (%))	80 (68)	73 (62)	0.410
Growth			
Weight (Kg)	8.30 ± 0.87	8.25 ± 0.86	0.688
Length (Cm)	69.9 ± 2.9	70.0 ± 2.8	0.952
Maternal characteristics			
Occupation (n (%) of workers)	101 (86)	102 (87)	0.314
Education (n (%) of high school)	33 (28)	34 (29)	1.000
Baseline iron status			
Hemoglobin (g/L)	111 ± 10.4	111 ± 10.0	0.877
Anemia (n (%))	57 (49)	53 (45)	0.694

† Plus-minus values are means ± SD.

Table 2. Adherence of infants to the intervention

Items	Fe group (n = 117)	Placebo group (n = 117)	*p*-value
Total recorded days (d)	149 ± 5†	149 ± 5	0.969
Total no. of days present (d)	109 ± 42.1	110 ± 40.4	0.863
Total meals consumed (time)	219 ± 84.2	220 ± 81	0.883
Meals not eat all or partly (time)	8.8 ± 15.7	5.8 ± 11.6	0.090
Total added iron consumed (mg)	1093 ± 421	-	-
Added iron consumed per a day (mg)	7.33 ± 2.80	-	-

† Plus-minus values are means ± SD.

Table 1. No significant differences between the groups in any demographic indices known to affect the iron status of the infants, of both the infants and mothers, were observed. The mean Hb concentrations of the two groups did not differ significantly before the intervention (Fe group 111 g/L, placebo group 111 g/L, p=0.877). No statistically significant differences were noted in the proportion of infants with anemia between the Fe and placebo groups.

Impact of iron fortification

Iron status of infants in the 2 groups was compared at the end of intervention (Table 2). Mean hemoglobin concentrations in the Fe group was significantly higher than in the control group after 6 months of intervention (Fe group 118 g/L, placebo group 110 g/L, p<0.001). The prevalence of infants with anemia in the Fe group was significantly lower compared with that in the control group (Fe group 24%, placebo group 48%, p<0.001). Serum ferritin values were also significantly different at the end of the study (Fe group 40.7 K/L, placebo group 26.8 K/L, p<0.001). Using the WHO cut off point of 12 mcg/L for iron deficiency, 6.3 % of infants in the Fe group were iron deficient compared with 28.6 % in placebo group. The proportion of infants with iron deficiency anemia (Hb <110 g/L, SF<12 mcg/L) in the Fe group was significantly lower compared with that in the placebo group (p<0.001).

Figure 2 shows the changes in prevalence of anemia in the two groups before and after intervention. The prevalence of anemia in the Fe group had significantly reduced after intervention, but the change in placebo group was not significant. The differences with regard to mean increases in weight, height and morbidity during the study period between the Fe and placebo groups were not significant (data not shown).

Adherence of infants to the iron fortified complementary food

None of the parents or nursery staff reported that any child had unpleasant responses to the fortified food (abdominal pain, decreased appetite, vomiting, diarrhea, constipation and increased crying or fussiness) over the study period. Table 3 indicates nursery attendance of the children and the consumption of fortified food during the six month intervention. The mean days of presence of a child in the nursery were similar in both groups and no significant differences were seen between two groups in total

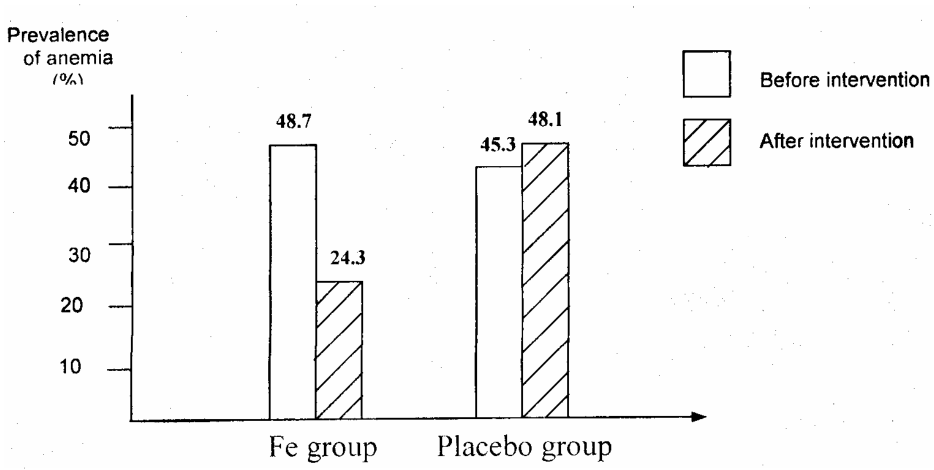

Figure 2. Changes in prevalence of anemia before and after intervention in both groups

Table 3. Effect of iron intervention on then iron status of infants in the study

Variable	Fe group (n)	Mean ± SD	Placebo group (n)	M±SD	*p*-value
Hemoglobin (g/L)	107	118 ± 11.7	104	110 ± 11.1	0.001
PCV	99	32.0 ± 2.29	97	31.3 ± 2.38	0.023
Serum ferritin (K/L)	96	40.7 ± 24.0	91	26.8 ± 21.4	0.001
Anemia† (n (%))	107	26 (24.3)	104	50 (48.1)	0.001
ID‡ (n(%))	96	6 (6.3)	91	26 (28.6)	0.001
IDA§ (n(%))	96	3 (3.1)	91	20 (22.0)	0.001

† Anemia: Hb<110 g/L; ‡ ID (Iron deficiency): SF<12 mcg/L; § IDA (Iron deficiency anemia): Hb<110g/L and SF<12 mcg/L

meal consumed in nursery and the mean number of meals that the infants did not eat. The mean amount of added iron that a child in the Fe group had over the study period was 1093 ± 421mg, corresponding to 7.33 ± 2.80mg per day.

DISCUSSION

This study shows that iron fortification of nursery food by adding ferrous sulphate to the water in which rice porridge is cooked improves the iron status of infants. Many studies have shown that iron status of young children was associated with demographic factors including gender, age, birth weight, length of gestation, breast-feeding and physiological size.[9] Socio-economic indices, dietary intake and morbidity are also determinants of iron deficiency.[8,10] In this study, all these confounding factors have been excluded by randomization at recruitment (Table 1). The design also excluded other uncommon factors like twins, low birth weight, congenital diseases, chronic diseases and severe anemia (Hb<90g/L). The differences in iron status between the two groups at the end of the study are due to the intervention.

At baseline, nearly half of the children (49% in Fe group and 45% in placebo group) were anemic (Hb<110 g/L) despite excluding infants with Hb<90 g/L. Anemia is a major problem for these children. This finding is consistent with other studies showing that there is a substantial risk of iron deficiency anemia after 6 months of age unless a source of extra iron is provided. This is due to the rapid growth of a child, depletion of iron stores, declining iron concentrations in breast milk and inadequate iron in the cereal that is traditionally used as a weaning food.[13-16]

The present study was designed to add 10 mg of elemental iron, as ferrous sulfate (50 mg ferrous sulfate per 100 g of dry rice) per infant per day, to rice porridge used as a complementary food in the nursery. The haemoglobin levels and serum ferritin levels were significantly higher in the Fe group than in the placebo group after 6 months of intervention. There were also significant differences between two groups with regard to the prevalence of ID and IDA. The prevalence of anemia was the same in both groups initially and did not change in the placebo group, but dropped significantly to 24.3% in the Fe group. This intervention significantly improved iron status. There was no report about any side effects or undesired response to the fortified food. Table 3 shows that the amount of staple food consumed and left over; and the mean days of study participation were similar in the two groups. This means our fortified food was acceptable to the children.

Overall, children consumed about 70% of the food offered, so the average amount of added iron a child took over the study period was 1093 ± 421 mg in the Fe group, corresponding to 7.33 ± 2.80 mg a day which is about 70% of the portion we offered. External factors contributed to this finding, mainly the large number of absences from the nursery over the summer school holidays. Lind[17] used a daily supplementation with 10 mg Fe in infants from 6 to 12 months of age, but found that no further effect was obtained beyond a total supplementation of 7mg per child per day. In line with his finding, we think that our fortification level supplied sufficient iron and a dose of 10 mg Fe/d per child will be sufficient in future national fortification programs. Despite many published studies on iron supplementation and fortification, there is no proven strategy that works. Iron supplementation is efficacious for improving IDA in infants, but has low adherence because of side effects such as vomiting and nausea [17,18] Iron fortification is effective and has less side effects.[19,20] The recently developed micro-encapsulated Sprinkles™ has been used successfully,[21-23] but is not practical in many developing countries because of cost, the technology needed and the problems of quality control and transport. However our nursery based iron-fortification should be cost-effective and feasible in the DPRK. The amount of fortified porridge offered is constant and gives infants a constant amount of added iron. The immediate use of the fortified food eliminates problems of storage and spoilage. Good results from clinical trials do not always predict a successful intervention programme. Clinical trials have higher adherence to the intervention than the actual program since the field researchers strictly control the intervention. In home-based interventions using iron supplementation or sprinkles, the main barriers to adherence are the trouble of administration, forgetfulness of caretaker and acceptance by the child. In contrast, this nursery-based fortification should have good adherence even in the real programme since the procedures of fortification and administration are easier and most nursery cooks and caretakers have a higher education level.

Our study differs from others in situation, sampling[I7,20] duration and materials,[20] but had similar improvements in measures of anaemia. Our results, in spite of some limitations, suggest further possible developments. Firstly, this result could be the basis for establishing a future national programme, perhaps with some changes. Adding vitamin C would increase the absorption of iron,[22] but might not be practicable because it is not locally available and may be destroyed by cooking. Many children were already anemic at the age of six months, so we should start supplementation with iron fortified foods before this age. Other studies[22] indicate that longer periods of supplementation give better results. We should also consider the necessity and possibility of co-fortification with other nutrients such as zinc.

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AUTHOR DISCLOSURES

HuiYong Rim, SuHuan Kim, ByongChel Sim, HaeYong Gang, HoYong Kim, YongRan Kim, RakChel Kim, MunHui Yang and SangPil Kim, no conflicts of interest.

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Institute of Child Nutrition, Academy of Medical Sciences Saesalim Dong, Tongdaewon District, Pyongyang, DPR of Korea

添加鐵副食品對北韓嬰兒鐵狀況之效應

本研究想了解在煮粥水中添加硫酸亞鐵，而讓嬰兒攝取米粥後，其體內鐵的狀況。自北韓 36 個育嬰所徵招年紀 6-12 個月大的嬰兒 234 位，隨機分配為鐵攝取組和安慰劑組。一開始，幾乎一半的嬰兒血紅素少於 110 g/L，而且兩組在基礎血紅素濃度和貧血盛行率上都沒有差異。鐵攝取組每天攝取含 10 毫克鐵的米粥，是將硫酸亞鐵加入水中，再用此水烹煮米粥，而安慰劑組則是攝取沒有強化過的粥。試驗期 6 個月後，測量血紅素、血清鐵蛋白和紅血球比容積。結果發現鐵攝取組比安慰劑組嬰兒貧血的比例較低，血紅素和血清鐵蛋白濃度較高，缺鐵性貧血率較低。硫酸亞鐵加入水中和米粥一起烹煮，能使北韓缺鐵性貧血嬰兒的盛行率降低且無有害副作用。這樣簡單的強化方法或許適用於北韓的全國性計劃和有大型育嬰所的其它國家。

關鍵字：鐵狀況、缺鐵性貧血、添加鐵、嬰兒、育嬰所食品