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Effects of iron fortification in a school feeding scheme and anthelmintic therapy on the iron status and growth of six- to eight-year-old schoolchildren

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Abstract

The effect of iron fortification of soup in a school feeding scheme (20 mg iron and 100 mg vitamin C per portion) and anthelmintic therapy on haematological and iron status and on growth was studied in 179 schoolchildren age six to eight years. Measurements were performed before and at the end of a six-month intervention and repeated five months later. In children with low baseline iron stores (serum ferritin <20 µg/L), iron fortification was associated with increases in haemoglobin ($p < .05$)*, mean corpuscular volume* ($p < .01$)*, and serum ferritin* ($p < .0001$)*, compared with children who received unfortified soup. Significant positive effects of the anthelmintic therapy on haemoglobin concentrations* ($p < .05$) *and height-for-age Z scores* ($p < .01$) *were found. Children with adequate baseline iron stores showed smaller but similar changes.*

Introduction

Iron deficiency is not life threatening, but it can have detrimental effects on work capacity, learning ability, and resistance to disease. These consequences can slow the development of schoolchildren [1]. For example, test scores were lower in iron-deficient than in iron-sufficient primary-school children [2]. Several studies reported improvements in a variety of measures of school performance after treatment with iron supplements, especially in anaemic children [3–5].

Iron deficiency is a common problem throughout childhood [6]. Studies in schoolchildren age 11 years or younger in South Africa showed that 4% to 36% were anaemic and 0% to 33% had iron deficiency [7–9].

Negative iron balance in primary-school children can be caused by low iron intake and low bioavailability of iron in the diet. School feeding programmes provide an excellent opportunity for supplying additional iron to the diet [6]. In one such programme in Chile, biscuits fortified with bovine haemoglobin (providing 1 mg absorbable iron/day) were given to children 6 to 12 years of age. After 15 months, haemoglobin (Hb) concentrations had increased significantly in children who received fortified biscuits compared with those who had unfortified biscuits [10].

Parasitic infection (hookworm and *Trichuris trichiura*) is a common cause of iron loss in children in Africa [1]. In communities with high prevalences of parasitic infections the effect of iron fortification or supplementation may be limited when it is not combined with anthelmintic therapy. Anthelmintic therapy alone improved iron status in schoolchildren in communities where parasitic (hookworm) infections were common [11].

In a pilot study in one school, soup fortified with iron to provide 1 mg absorbable iron per day and vitamin C 100 mg was given to 6- to 12-year-olds. Baseline mean iron intake in those age 8 to 12 years was 8.0 ± 2.8 mg (0.6 ± 0.2 mg absorbable iron) per day. After a four-month intervention, the children's iron status was significantly improved [12].

The aims of this clinical trial were to determine the separate and combined effects of iron-fortified soup in a school feeding scheme and anthelmintic therapy on the haematological, iron, and anthropometric

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status in six- to eight-year-old schoolchildren living in low socio-economic communities.

Methods

Study population

Sixty-five pupils in their first year of school were randomly selected from each of five primary schools (three in the town, two in the surrounding farming areas) in subeconomic communities of mixed ethnic origin (European-African-Malay) in the Worcester region, approximately 100 km north of Cape Town, South Africa. The schools were included in the Peninsula School Feeding Scheme. Exclusion criteria were age 9 years and older, current use of iron supplements, inclusion in an iron-fortification trial the previous year, and infection (white blood cell count above the normal range: >14.5/dl for children age 5 to 7 years, >13.5/dl for those age 8 to 11 years [13].

Of the 247 children included in the study, 179 (96 boys, 83 girls) had complete haematological data for all three surveys. Stool specimens for parasitologic examination were obtained from 155 children at baseline, and 134 children provided stool specimens at each of the three surveys.

Written informed consent was obtained from the parent or guardian of each participant. The study was approved by the ethics committee of the South African Medical Research Council. Permission for the study was also obtained from the Department of Education and Culture, the management committee of the Peninsula School Feeding Association, and the principal of each school.

Study design

During the intervention period, three experimental schools received fortified soup powder, and two control schools received unfortified soup powder. One experimental and one control school were situated in a farming community. The subjects in each school were randomly assigned to one of two groups; one received anthelmintic therapy and the other a placebo. The treatment groups received iron-fortified soup and anthelmintic therapy (FeA), iron-fortified soup and a placebo (FeP), unfortified soup and anthelmintic therapy (BA), and unfortified soup and a placebo (no intervention, BP).

School feeding and iron fortification

At the beginning of the study, the School Feeding Scheme issued one cup (±160 ml) of soup, a slice of brown bread, and 5 ml peanut butter per pupil per day. Four weeks after baseline, the School Feeding Scheme doubled the portions of bread and peanut butter. Teachers, mothers of the children, or paid women from the community prepared the soup and bread according to instructions. The soup and bread were distributed to the children on school days under supervision of the teachers.

The soup was fortified with ferrous fumarate 60 mg to provide 20 mg elemental iron per portion and vitamin C 100 mg per portion. The school staff did not know which type of soup the school had received. The intervention lasted six months (June–November).

A 30-g sample was taken at the school from each 25-kg bag of soup powder and analysed for iron content by atomic absorption spectroscopy. The iron content of the soup powder of the experimental and control schools was 1,491 ± 33 mg/kg ($n = 17$) and 72 ± 15 mg/kg ($n = 11$), respectively, or 18.4 ± 0.4 mg and 0.9 ± 0.2 mg iron per portion, respectively. The estimated additional absorbable iron provided by the fortified soup was thus 0.9 mg per day. Even with low dietary iron intake, the total absorbable iron intake of a child receiving the fortified soup would have exceeded the WHO recommendation of 1 mg per day for a child age 1 to 12 years [14].

Anthelmintic therapy

Treatment consisting of two 200-mg albendazole tablets (Zentel) was given to the children after the baseline survey (June 1993) and repeated four months later (October 1993). The tablets were taken under the supervision of a medical doctor or teachers.

Measurements

Anthropometric, biochemical, haematological, and parasitological measurements were performed and demographic information was obtained during the baseline survey (May 1993). These measurements were repeated at the end of the six-month intervention (November 1993) and again after a five-month non-intervention period (May 1994).

The pupils were weighed in light clothing (without shoes, jacket, or jersey) to the nearest 0.1 kg on a calibrated electronic load cell scale. Height was measured to the nearest 0.1 cm using a metal tape measure that was fitted to the wall.

Venous blood was collected from the antecubital vein of each child and was aliquoted in tubes with and without the anticoagulant ethylenediaminetetraacetic acid (EDTA). Haematological analyses (full blood count, differential white blood cell count) were performed within eight hours on a Technicon H2. Serum ferritin concentration was determined by immunoradiometric assay, and radioactivity was determined in a crystal multidetector gamma counter. Serum iron concentration was determined spectrophotometrically with a Technicon RA-1000 automated system using a colourimetric method without deproteinization. Total iron-binding capacity (TIBC) was determined by the same method after saturation of transferrin with iron and precipitating uncomplexed iron with magnesium carbonate. Transferrin saturation was calculated by expressing total serum iron as a percentage of TIBC. Red blood cell folate concentration was analysed using the SimulTRAC-SNB radioassay kit for vitamin B_{12} [^{57}Co]/folate [^{125}I]. Plasma albumin concentration was determined using the bromcresol-green method.

Stool samples were collected during school hours and preserved in 10% formol saline (10% formalin in 0.9% sodium chloride). The specimens were emulsified in formol saline, and an aliquot was jet washed with tap water through a Visser filter made of two mesh cloth filter bags with 80- and 25-μm pore size, the former within the latter. One drop of the resultant filtrate was placed under a 22 x 22-mm coverglass and examined microscopically at ×100 magnification. Cyst identity was confirmed at ×250 magnification.

During the intervention, the teachers recorded the number of days that each child consumed the soup. Individual attendance records were obtained from the school registers at the end of the study period.

Reference standards

The height and weight measurements were evaluated using the percentiles of the National Center for Health Statistics [15]. The age-specific lower limits or ranges were used to classify the results for haematological parameters and iron status measurements, since these values are age dependent during childhood [16]: low Hb concentration below 11.5 g/dl for ages 5 to 7 years and below 12.0 g/dl for ages 8 to 11 years; low mean corpuscular volume (MCV) below 75 fl for ages 5 to 7 years and below 76 fl for ages 8 to 11 years [17]; 95% ranges: mean corpuscular Hb (MCH) 25 to 31 pg for ages 6 to 8 years and 26 to 32 pg for ages 9 to 11 years; serum iron 6.1 to 27.4 mmol/L for ages 6 to 8 years and 7.3 to 27.0 mmol/L for ages 9 to 11 years; TIBC 53.7 to 82.6 mmol/L for ages 6 to 8 years and 53.6 to 84.5 mmol/L for ages 9 to 11 years; and transferrin saturation 11% to 43% for ages 6 to 11 years [16]. The WHO criterion for anaemia (Hb <12 g/dl)[18] was also used to compare with results of studies using this cut-off point. For ferritin concentrations, 10 μg/L was considered the lower limit of normal [19]. Red blood cell folate concentrations below 120 μg/L indicate folate deficiency. Serum albumin concentrations below 35 g/L are considered subnormal.

Statistical evaluation

Children in each of the four treatment groups were subdivided into those with low (serum ferritin <20 μg/L) and adequate (serum ferritin ≥20 μg/L) iron stores at baseline. Ferritin concentrations below 20 μg/L were considered diagnostic of iron deficiency, because anaemic patients with such low values respond to oral iron therapy [20]. The baseline results of children with low iron stores were compared with those of children with adequate iron stores using the Wilcoxon two-sample test. This test was also used to compare children with and without parasitic infections, and those infected with *Trichuris trichiura* with children infected with other parasites, regarding baseline results.

Changes in each of the parameters from baseline to the end of the six-month intervention and from baseline to 11 months later (i.e., 5 months after intervention) were calculated. The changes were used to evaluate the effects of iron fortification and anthelmintic therapy and their interaction on children with low or adequate iron stores by analysis of variance. The effects of the treatments on the prevalences of parasitic species were evaluated using repeated measures analysis for categorical data.

The experimental factors were anthelmintic therapy, iron-fortified soup, and time. The analysis was done for the full model, which included the main effects of the three experimental factors and their interactions. The outcome modeled was the marginal probabilities of the prevalences of the parasites. The interaction terms of anthelmintic therapy with time, iron-fortified soup with time, and anthelmintic therapy with iron-fortified soup with time were of interest to see whether the treatments had significant effects relative to the initial prevalences of the parasites. Probability values below .05 were considered statistically significant.

Results

At baseline, 23.5% (42/179) of the children were anaemic according to age-specific cut-off points [16], and 42.5% (76/179) could be classified as anaemic using WHO cut-off points [18]. Hypochromia (low MCH) was observed in 10.6% (19/179) of the children, but only 2.2% (4/179) had microcytosis (low MCV). Iron deficiency, indicated by low serum ferritin concentrations (15.6%, 28/179) and low transferrin saturation (25.3%, 44/174), was common; one child (0.6%) had folate deficiency. Stunting (height-for-age *Z* scores < -2 SD) and underweight (weight-for-age *Z* scores < -2 SD) were found in 17.9% (32/179) and 14.0% (25/179) of the children, respectively.

Table 1 compares the baseline anthropometric,

TABLE 1. Anthropometric, haematological, and iron status results at baseline in six- to eight-year-old schoolchildren with low and adequate iron stores

Measurements	Low iron stores (n = 72) Mean	Low iron stores (n = 72) SD	Adequate iron stores (n = 106) Mean	Adequate iron stores (n = 106) SD	p
Age (yr)	6.9	0.5	7.0	0.5	.4339
Weight (kg)	19.1	2.6	19.6	2.3	.2264
Height (cm)	113.8	5.2	115.5	4.6	.0432
WAZ	−1.23	0.95	−1.00	0.82	.1364
HAZ	−1.34	0.93	−1.01	0.87	.0256
WHZ	−0.53	0.84	−0.49	0.79	.6154
Hb (g/dl)	12.0	0.8	12.3	0.8	.0124
MCV (fl)	83.3	4.4	83.3	3.5	.9421
MCH (pg)	26.9	1.6	26.9	1.4	.8391
RDW	13.4	0.8	13.0	0.8	.0004
WCC ($\times 10^9$/L)	8.4	2.2	8.6	2.1	.4356
Ferritin (μg/L)	12.1	4.8	37.7	16.9	.0001
Serum iron (mmol/L)	10.8	4.2	11.5	6.3	.6227
TIBC (mmol/L)	65.9	10.1	62.1	9.3	.0011
TS (%)	17.1	7.8	19.0	10.3	.2248
RBC folate (μg/L)	310	86	336	99	.0732
Albumin (g/L)	48.3	2.5	48.5	3.0	.3295

WAZ, Weight-for-age Z score; HAZ, height-for-age Z score; WHZ, weight-for-height Z score; Hb, haemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; RDW, red cell distribution width; WCC, white cell count; TIBC, total iron-binding capacity; TS, transferrin saturation; RBC, red blood cell.

haematological, and biochemical results of children with low iron stores (serum ferritin <20 μg/L) with those with adequate iron stores (serum ferritin ≥20 μg/L). Children with low iron stores had lower ($p < .05$) heights, height-for-age Z scores, and Hb concentrations, and higher ($p \leq .001$) red cell distribution width (RDW) and TIBC than those with adequate iron stores.

The records showed that the children consumed the soup on a regular basis. Of the days on which the soup was available, the average percentage of days that soup was consumed by the children were 87 ± 27% in the FeA group, 91 ± 22% in the FeP group, and 97 ± 5% in both the BA and the BP groups.

Table 2 shows the haematological and iron status parameters before intervention (baseline), the changes from baseline to the end of the six-month intervention, and the changes from baseline to five months after the intervention in children with low baseline iron status. Iron fortification was associated with increases in MCV ($p = .0065$) and serum ferritin ($p = .0001$) during intervention, compared with children who received unfortified soup. Hb concentrations remained constant in the children who received fortified soup but decreased in those who received unfortified soup ($p = .0193$). The TIBC tended to decrease more in groups that received iron fortification than in those that received the unfortified soup, although differences were not significant.

Anthelmintic therapy was associated with positive changes in Hb ($p = .0393$) compared with the placebo. Interaction between the effects of iron fortification and anthelmintic therapy was observed for MCH ($p = .0311$), serum ferritin ($p = .0060$), and transferrin saturation ($p = .0097$). Significant effects were observed five months after the intervention concerning increases in serum ferritin ($p = .0176$) associated with iron fortification, and in MCH ($p = .0053$) associated with anthelmintic therapy. White cell counts decreased in all groups during the intervention but increased again after the intervention.

Table 3 gives the haematological and iron status parameters at baseline, the changes from baseline to the end of the intervention, and the changes from baseline to five months after the intervention in children with adequate baseline iron stores. Iron fortification was associated with significant increases in MCV ($p = .0029$) during intervention, compared with children who received unfortified soup. In these two groups, the mean serum ferritin remained constant and decreased, respectively ($p = .0403$). Significantly larger increases in transferrin saturation ($p = .0035$) were observed five months after the intervention in children who received unfortified

TABLE 2. Haematological and iron status at baseline, changes from baseline to the end of intervention, and changes from baseline to five months after intervention in children with low baseline iron stores

Treatment group	Hb (g/dl)	MCV (fl)	MCH (pg)	Ferritin (μg/L)	TIBC (mmol/L)	TS (%)	WCC (×10⁹/L)
Baseline (0 mo)							
FeA (*n* = 20)	12.1 (0.9)	83.3 (2.7)	27.2 (0.9)	11.4 (4.3)	66.2 (6.9)	15.9 (5.5)	8.3 (2.7)
FeP (*n* = 24)	12.2 (0.7)	84.4 (4.7)	27.3 (1.7)	13.2 (5.0)	65.1 (14.7)	20.3 (9.7)	8.5 (2.0)
BA (*n* = 15)	11.6 (0.8)	81.2 (5.3)	25.9 (1.7)	11.5 (4.6)	64.5 (4.6)	18.5 (5.0)	8.1 (1.7)
BP (*n* = 14)	11.7 (0.9)	82.7 (5.2)	26.4 (2.1)	11.5 (5.7)	67.7 (8.7)	11.8 (6.6)	8.3 (1.7)
Change from baseline to the end of intervention (6 mo)							
FeA (*n* = 20)	0.1 (0.7)	1.9 (1.8)	0.6 (0.6)	8.1 (9.6)	−3.1 (6.5)	6.9 (8.3)	−0.7 (1.9)
FeP (*n* = 24)	−0.1 (0.5)	1.7 (1.5)	0.8 (0.9)	18.2 (12.2)	−2.0 (16.2)	−1.3 (13.4)	−0.1 (2.5)
BA (*n* = 15)	−0.2 (0.6)	0.7 (1.3)	0.9 (0.7)	2.5 (10.5)	4.5 (8.4)	5.0 (13.7)	−0.8 (1.1)
BP (*n* = 14)	−0.5 (0.6)	0.8 (1.0)	0.2 (0.8)	−1.5 (6.7)	−1.8 (11.6)	11.9 (8.8)	−0.5 (2.1)
Change from baseline to 5 mo after intervention (11 mo)							
FeA (*n* = 20)	0.7 (0.7)	0.7 (2.4)	−0.2 (0.9)	5.7 (8.0)	7.6 (5.6)	4.6 (8.7)	0.6 (1.8)
FeP (*n* = 24)	0.2 (0.6)	0.4 (1.3)	−0.6 (0.5)	6.0 (9.7)	0.2 (17.4)	3.7 (15.7)	0.0 (2.3)
BA (*n* = 15)	0.3 (0.6)	0.4 (1.3)	−0.4 (0.7)	2.9 (7.6)	6.7 (8.3)	2.5 (5.4)	0.2 (1.8)
BP (*n* = 14)	0.2 (0.6)	−0.7 (1.1)	−1.0 (0.6)	−0.9 (5.6)	5.5 (12.1)	6.7 (8.4)	1.0 (1.9)

Hb, Haemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; TIBC, total iron-binding capacity; TS, transferrin saturation; WCC, white cell count; Fe, iron-fortified soup; B, unfortified soup; A, anthelmintic therapy; P, placebo. Values are means and (SD).

TABLE 3. Haematological and iron status at baseline, changes from baseline to the end of intervention, and changes from baseline to five months after intervention in children with adequate baseline iron stores

Treatment group	Hb (g/dl)	MCV (fl)	MCH (pg)	Ferritin (μg/L)	TIBC (mmol/L)	TS (%)	WCC (×10⁹/L)
Baseline (0 mo)							
FeA (*n* = 30)	12.5 (0.9)	83.0 (3.5)	26.9 (1.7)	39.9 (21.7)	64.6 (10.9)	21.2 (10.3)	8.6 (2.1)
FeP (*n* = 30)	12.3 (0.9)	83.6 (3.3)	27.1 (1.2)	37.7 (14.6)	62.2 (10.3)	20.1 (9.9)	8.5 (2.1)
BA (*n* = 22)	12.4 (0.8)	83.9 (3.6)	27.1 (1.3)	33.4 (12.1)	61.6 (5.9)	15.7 (9.6)	8.7 (1.8)
BP (*n* = 23)	12.1 (0.8)	82.7 (3.6)	26.7 (1.6)	39.3 (17.3)	59.0 (8.1)	18.5 (11.0)	8.6 (2.3)
Change from baseline to the end of intervention (6 mo)							
FeA (*n* = 30)	−0.1 (0.7)	1.9 (1.7)	0.6 (0.8)	−2.0 (24.3)	−0.2 (10.6)	3.3 (11.3)	−1.2 (2.1)
FeP (*n* = 30)	0.0 (0.5)	1.6 (1.5)	0.5 (0.6)	0.0 (19.9)	0.1 (10.8)	4.9 (13.7)	−0.6 (2.4)
BA (*n* = 22)	−0.3 (0.6)	0.5 (1.8)	0.6 (0.6)	−6.3 (18.1)	2.1 (4.0)	6.9 (8.2)	−0.2 (2.1)
BP (*n* = 23)	0.0 (0.6)	1.0 (1.5)	0.7 (0.9)	−12.2 (15.6)	3.9 (8.7)	3.0 (11.1)	−0.9 (2.3)
Change from baseline to 5 mo after intervention (11 mo)							
FeA (*n* = 30)	0.5 (0.7)	0.3 (1.5)	−0.6 (0.8)	−10.8 (20.1)	15.8 (34.8)	2.1 (11.4)	0.1 (2.3)
FeP (*n* = 30)	0.4 (0.6)	0.1 (1.3)	−0.7 (0.6)	−4.4 (20.9)	5.6 (13.4)	1.8 (11.1)	0.6 (2.3)
BA (*n* = 22)	0.2 (0.6)	−0.4 (0.9)	−0.8 (0.5)	−6.9 (20.3)	6.4 (12.2)	11.0 (10.2)	0.0 (2.1)
BP (*n* = 23)	0.3 (0.8)	0.2 (1.8)	−1.0 (1.3)	−7.9 (5.6)	5.7 (9.5)	6.2 (11.2)	0.5 (2.1)

See table 2 for abbreviations.

Values are means and (SD).

TABLE 4. Anthropometric measurements at baseline, changes from baseline to the end of intervention, and changes from baseline to five months after intervention in children with adequate baseline iron stores

Treatment group	Weight (kg)	Height (cm)	Weight-for-age *Z* score	Height-for-age *Z* score	Weight-for-height *Z* score
Baseline (0 mo)					
FeA (*n* = 20)	19.3 (1.9)	114.8 (3.7)	−1.18 (0.70)	−1.20 (0.74)	−0.54 (0.53)
FeP (*n* = 24)	18.9 (2.2)	112.8 (4.4)	−1.22 (0.87)	−1.47 (0.83)	−0.38 (0.90)
BA (*n* = 15)	20.1 (3.6)	115.3 (7.5)	−0.96 (1.25)	−1.16 (1.25)	−0.33 (0.93)
BP (*n* = 14)	17.7 (2.3)	112.5 (5.2)	−1.70 (0.94)	−1.55 (0.93)	−1.02 (0.83)
Change from baseline to the end of intervention (6 mo)					
FeA (*n* = 20)	1.3 (0.8)	3.1 (0.7)	0.07 (0.23)	0.06 (0.13)	0.07 (0.34)
FeP (*n* = 24)	0.9 (0.7)	2.9 (0.7)	−0.03 (0.22)	0.04 (0.13)	−0.04 (0.27)
BA (*n* = 15)	0.9 (0.4)	3.3 (0.7)	−0.04 (0.18)	0.09 (0.15)	−0.12 (0.28)
BP (*n* = 14)	1.0 (0.5)	2.2 (1.0)	0.03 (0.18)	−0.1 (0.18)	0.15 (0.28)
Change from baseline to 5 mo after intervention (11 mo)					
FeA (*n* = 20)	2.8 (1.1)	6.1 (1.2)	0.22 (0.23)	0.13 (0.21)	0.25 (0.38)
FeP (*n* = 24)	2.3 (0.7)	5.6 (1.2)	0.07 (0.23)	0.06 (0.23)	0.15 (0.29)
BA (*n* = 15)	2.5 (0.7)	5.8 (0.9)	0.09 (0.24)	0.09 (0.20)	0.10 (0.26)
BP (*n* = 14)	2.2 (0.6)	5.1 (1.1)	0.12 (0.17)	−0.03 (0.15)	0.25 (0.25)

See table 2 for abbreviations.

Values are means and (SD).

soup than in those who received fortified soup. The same trend in white cell count was observed as in children with low baseline iron stores.

Table 4 shows the anthropometric results at baseline, the changes from baseline to the end of the intervention, and the changes from baseline to five months after the intervention in children with low baseline iron stores. Anthelmintic therapy was associated with greater increases in height ($p = .0015$) and height-for-age Z scores ($p = .0027$) compared with a placebo. Significant interaction between iron fortification and anthelmintic therapy was observed for height ($p = .0263$), height-for-age Z scores ($p = .0154$), and weight-for-height Z scores ($p = .0087$). Five months after the intervention, the children who were treated had greater increases in height ($p = .0344$) and weight ($p = .0346$) than those who received the placebo.

In table 5 the anthropometric results at baseline, the changes from baseline to the end of the intervention, and the changes from baseline to five months after the intervention in children with adequate baseline iron stores are given. Neither anthelmintic therapy nor iron fortification alone was associated with significant effects on these parameters. Significant interaction between these two interventions for weight ($p = .0208$) and weight-for-age Z scores ($p = .0262$) was observed during and after the intervention ($p = .0099$ and .0115, respectively).

Parasitic infections were found in 58.7% (91/155) of the children. Height-for-age Z scores at baseline were lower ($p = .0018$) in children with parasitic infections ($n = 91$; -1.35 ± 0.87) than in those without infection ($n = 64$; -0.88 ± 0.88). *Trichuris trichiura*, *Ascaris lumbricoides*, and *Hymenolepis nana* were the most common parasitic species at baseline in this population, with prevalences of 38.1% (59/155), 20.0% (31/155), and 20.7% (32/155), respectively. At baseline 33.9% of the 59 children infected with *T. trichiura* were anaemic, compared with 9.4% of the 32 infected with parasites other than *Trichuris*. Hb concentrations tended to be lower in children with *Trichuris* infection (12.0 ± 0.9 g/dl vs 12.4 ± 0.7 g/dl, $p = .0541$). The MCH (26.7 ± 1.6 pg vs 27.4 ± 1.3 pg, $p = .0245$), MCH concentration ($32.1 \pm 0.9\%$ vs $32.7 \pm 0.7\%$, $p = .0004$), and serum iron concentration (10.8 ± 5.1 mg/dl vs 13.0 ± 5.6 mg/dl, $p = .0462$) were lower and RDW (13.4 ± 1.0 μm vs 12.8 ± 0.6 μm, $p = .0013$) was higher in children with *Trichuris* infection compared with those infected with other parasites.

The prevalence of infection with more than one parasitic species decreased from baseline to the end of intervention in the groups that received anthelmintic treatment: FeA 15.9% (7/44) to 4.9% (2/41), and BA 31.4% (11/35) to 8.6% (3/35). It remained high in the placebo groups: FeP 12.5% (6/48) to 17.0% (8/47), and BP 39.3% (11/28) to 32.3% (10/31).

TABLE 5. Anthropometric measurements at baseline, changes from baseline to the end of intervention, and changes from baseline to five months after intervention in children with adequate baseline iron stores

Treatment group	Weight (kg)	Height (cm)	Weight-for-age *Z* score	Height-for-age *Z* score	Weight-for-height *Z* score
Baseline (0 mo)					
FeA (*n* = 30)	20.0 (2.5)	116.8 (4.7)	−0.92 (0.92)	−0.81 (0.84)	−0.56 (0.84)
FeP (*n* = 30)	19.7 (2.0)	115.8 (4.2)	−0.84 (0.74)	−0.86 (0.86)	−0.42 (0.66)
BA (*n* = 22)	18.9 (1.9)	113.6 (4.3)	−1.23 (0.67)	−1.34 (0.60)	−0.50 (0.79)
BP (*n* = 23)	19.8 (2.5)	115.5 (4.8)	−1.06 (0.89)	−1.15 (0.86)	−0.43 (0.89)
Change from baseline to the end of intervention (6 mo)					
FeA (*n* = 30)	1.4 (0.6)	3.1 (0.7)	0.08 (0.13)	0.06 (0.12)	0.07 (0.24)
FeP (*n* = 30)	1.2 (0.6)	2.9 (0.9)	0.03 (0.21)	0.02 (0.16)	0.07 (0.34)
BA (*n* = 22)	0.9 (0.5)	2.9 (0.7)	−0.04 (0.17)	0.04 (0.11)	−0.06 (0.23)
BP (*n* = 23)	1.4 (0.8)	3.1 (0.6)	0.09 (0.24)	0.07 (0.10)	0.08 (0.36)
Change from baseline to 5 mo after intervention (11 mo)					
FeA (*n* = 30)	2.9 (1.1)	5.8 (0.9)	0.15 (0.17)	0.06 (0.13)	0.21 (0.29)
FeP (*n* = 30)	2.6 (0.8)	5.8 (1.0)	0.06 (0.23)	0.05 (0.19)	0.12 (0.30)
BA (*n* = 22)	2.2 (0.6)	5.5 (0.9)	0.02 (0.22)	0.03 (0.16)	0.08 (0.28)
BP (*n* = 23)	3.0 (1.6)	5.8 (0.8)	0.19 (0.34)	0.08 (0.12)	0.25 (0.44)

See table 2 for abbreviations.

Values are means and (SD).

Figure 1 shows the effect of intervention on the prevalence of the three most common parasites in the 134 children with complete parasitological data. The prevalence of *T. trichiura* tended to decrease in all groups during the study period. The prevalence of *A. lumbricoides* decreased in the FeA and BA groups during intervention compared with the FeP and BP groups. In the anthelmintic therapy groups, the prevalence of *Ascaris* increased again after intervention to nearly baseline values. The prevalence of *H. nana* decreased in the FeA group but increased in the BA group during intervention. The prevalences of *Giardia lamblia* (3.9%, 6/155), *Enterobius vermicularis* (1.9%, 3/155), and hookworm (1.3%, 2/155) were low at baseline and remained below 5% throughout the study.

Of the three most common parasites, only *A. lumbricoides* showed significant treatment effects. Table 6 gives the analysis of weighted least-squares estimates for changes in the prevalence of this parasite from baseline to the end of intervention and for changes from the end of intervention to five months after intervention. Anthelmintic therapy significantly reduced the prevalence of *Ascaris* during intervention ($p = .0226$), but with cessation of therapy after the intervention the prevalence increased significantly ($p = .0124$).

A significant improvement in school attendance was associated with iron fortification ($p = .0276$) in children with low baseline iron stores. The percentage of days that these children were absent during the intervention period was 2.8% and 2.0% for the FeA and FeP groups, and 4.4% and 4.8% for the BA and BP groups, respectively. In children with adequate iron stores, the percentage days of absence was 2.2%, 3.5%, 3.5%, and 4.2% for the FeA, FeP, BA, and BP groups, respectively, during the intervention. After the intervention, the rates of absenteeism were similar for all the groups.

Discussion

Baseline status

The high prevalence of anaemia of 42.5% according to WHO criteria, which we observed in children age 6 to 8 years, is in agreement with that estimated for ages 5 to 12 years in Africa (49%) [21]. These prevalences were higher than the 6% to 18% reported for 6- to 11-year-olds of mixed ethnic origin in other areas of the Cape Province [7, 22]. Iron deficiency, as indicated by high prevalences of low serum ferritin (15.6% < 10 μg/L) and low transferrin saturation (25.7% <11%), was the major cause of anaemia in the present study. The finding of significantly lower heights and height-for-age *Z* scores in children with low iron stores adds to the evidence of the inhibit-

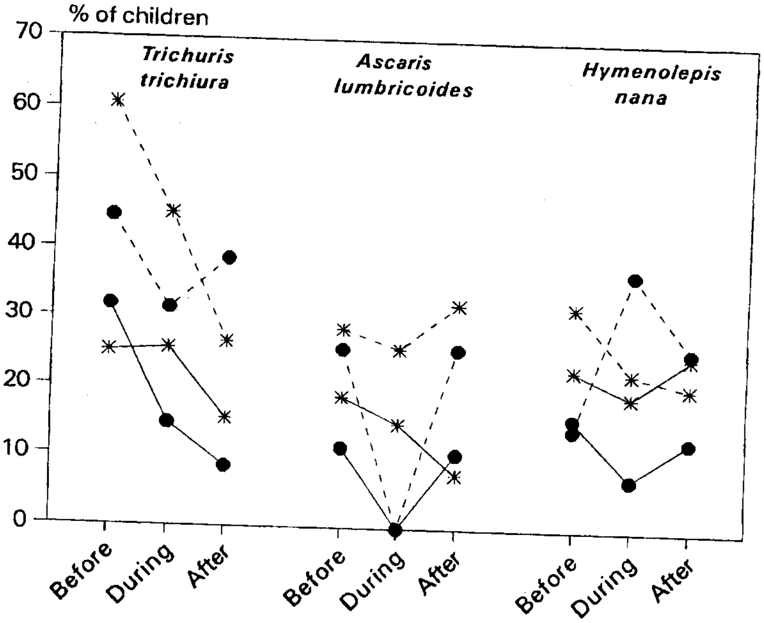

FIG. 1. The prevalences of *Trichuris trichiura*, *Ascaris lumbricoides*, and *Hymenolepis nana* in six- to eight-year-old schoolchildren before, during, and after intervention. Anthelmintic therapy: solid line with dots = iron-fortified soup; broken line with dots = unfortified soup. Placebo: solid line with stars = iron-fortified soup; broken line with stars = unfortified soup

ing effect micronutrient deficiencies have on growth [23, 24].

Our results indicated that the high prevalence of parasitic infections (58.7%) probably also contributed to the prevalence of stunting, underweight, and iron deficiency in these children, probably due to malabsorption, diarrhoea, and blood loss [25]. This was confirmed by the finding that these children had lower height-for-age *Z* scores than children without infection. Infection with *T. trichiura*, the most common parasite in these children, was associated with higher prevalences of anaemia and hypochromia (indicating iron deficiency), similar to that described during intense *Trichuris* infections (10,000 eggs/g stool) [26]. Daily iron losses may reach more than 1 mg in severe *Trichuris* infections [27]. In the present study hookworm infection was not common.

Effect of iron fortification

Iron-fortified soup providing 18.4 mg elemental iron or 0.9 mg absorbable iron per school day was associated with positive changes in Hb, MCV, and serum ferritin after the intervention. The effect was greater in children with low baseline iron stores than in those with adequate iron stores. Five months after the intervention, the positive effect of iron fortification on serum ferritin was still significant in children with low baseline iron stores.

In a pilot study with the same fortified soup, significant improvements in serum ferritin, but not in Hb, were observed within four months [12]. That intervention period may have been too short, however, since iron status does not change as rapidly with fortification as it does with supplementation [28]. In a trial in Chile using Hb-fortified chocolate biscuits (providing 1 mg absorbable iron) in a school feeding scheme, improvement in Hb was observed after 15 months [10]. In studies in which iron supplementation with higher doses (32–56 mg elemental iron/day) was given to schoolchildren, haematological and iron status values improved within two to four months [4, 5, 11].

Transferrin saturation increased equally in all treatment groups during intervention. Possibly a decrease in the rate of viral and bacterial infections (indicated by the lower white cell counts) had a greater effect on transferrin saturation than the additional iron intake. The post-intervention survey was conducted during summer, when the prevalence of infection tends to be low. Infection and iron deficiency are both associated with decreased transferrin saturation, but they have opposite effects on TIBC; infection is associated with decreased, and iron deficiency with increased, TIBC [29]. In children with

TABLE 6. Analysis of weighted least-squares estimates for the effects of anthelmintic therapy (A), iron fortification (Fe), and time, and their interactions on the prevalence of *Ascaris lumbricoides*

Treatment effect	Estimate	Standard error	p
Change from baseline to the end of intervention			
Intercept	0.8174	0.0267	.0000
A	−0.0614	0.0267	.0214
Fe	−0.0532	0.0267	.0463
Time	−0.0513	0.0176	.0036
A with Fe	−0.0131	0.0267	.6239
A with time	0.0402	0.0176	.0226
Fe with time	−0.0132	0.0176	.4546
A with Fe with time	0.0243	0.0176	.1683
Change from the end of intervention to 5 months after intervention			
Intercept	0.8344	0.0257	.0000
A	−0.0593	0.0257	.0213
Fe	−0.0707	0.0257	.0060
Time	0.0343	0.0170	.0428
A with Fe	−0.0319	0.0257	.2145
A with time	−0.0424	0.0170	.0124
Fe with time	0.0307	0.0170	.0698
A with Fe with time	−0.0055	0.0170	.7480

low baseline iron stores who received iron fortification, TIBC tended to decrease, indicating improved iron status, whereas in those who received unfortified soup, it tended to increase. In a population where infection is common, it is advisable to use transferrin saturation in combination with TIBC to evaluate iron status [29].

Iron fortification alone did not have a significant effect on growth or weight gain in this study. Studies in Indonesia [30] and Kenya [31] showed positive effects of iron supplementation on weight gain in deficient children. In the Indonesian study, iron supplementation was also associated with faster growth in anaemic children compared with a control group [30]. Interventions with single nutrients produced conflicting results concerning their ability to reduce stunting. Possible explanations for this are the existence of several growth-limiting nutrient deficiencies in the same children, and different study periods, doses of iron, and degrees of iron deficiency [23]. In contrast to the findings of another group [32], we did not observe a negative effect of additional iron on weight gain in children with adequate iron stores. This lack of a negative effect may be due to the lower dose of iron used (±1 mg/kg/day vs 3 mg/kg/day) or the greater age of the children (6–8 yr vs 12–18 mo).

The decrease in absenteeism with iron fortification in children with low baseline iron stores is significant, because school attendance affects school achievement. A possible reason for this decrease is the lower rates of viral and bacterial infections. Much controversy exists regarding the effect of iron deficiency on infection. However, abnormalities in cell-mediated immunity, neutrophil function, and secretory response of macrophages were found in the presence of iron deficiency [33].

Effect of anthelmintic therapy

The prevalence of *Trichuris* infection decreased in the groups that received anthelmintic therapy; however, a larger dose or follow-up treatment may be necessary to eradicate this parasite. The treatment was very effective in decreasing the prevalence of *Ascaris*. Reinfection of treated children with *Ascaris* to the baseline level occurred within five months, which is in agreement with the reinfection rate (6–8 mo) reported earlier [34]. Regular four-monthly anthelmintic treatment, as was given in the intervention period of the present study, decreased the prevalence of *Ascaris* effectively, whereas six-monthly treatments reduced the intensity (worm load), but not the prevalence of parasitic infections [35].

The association between anthelmintic therapy and Hb in children with low baseline iron stores was significant and was reasonably assumed to be due to the reduction in *Trichuris* infection. Other studies of worm treatment that positively affected Hb and iron status were mostly in communities with a high prevalence of hookworm infection [2, 11].

Children with low baseline iron stores experienced improved growth after anthelmintic therapy. Five months after intervention, their weight gain was also significantly improved. This is in agreement with the reported positive effect of anthelmintic treatment on weight gain [36-38] and growth [38]. These positive effects can be expected with reduction in diarrhoea, anorexia, malabsorption, and iron loss caused by parasitic infections [25].

Effect of a combination of iron fortification and anthelmintic therapy

Significant combined effects of iron fortification and anthelmintic therapy, over and above the effect of each treatment alone, were observed in MCH and iron status in children with low baseline iron stores. In populations in which parasitic infections are common, increased iron intake has a limited effect on the improvement of anaemia if it is not combined with deworming [2, 28].

Height and *Z* scores for height-for-age and weight-for-height increased significantly more in children with low baseline iron stores when the two treatments were combined. Although iron fortification alone did not have a significant effect on linear growth, it enhanced the effect of anthelmintic therapy in these children. This adds to the evidence that iron deficiency was a limiting factor in their growth. In children with adequate iron stores, in whom iron deficiency was probably not a limiting factor for growth, the combined treatment resulted in improvements in weight and weight-for-age *Z* scores.

Conclusion

This study showed that iron deficiency, parasitic infections, and possibly stunting in school-age children can be addressed effectively with iron fortification of soup in a school feeding scheme combined with regular anthelmintic therapy. Decreases in the prevalence of iron deficiency and parasitic infections improve not only children's physical well-being, but probably also their ability to learn [39]. School feeding schemes for iron fortification have the benefits of a regulated intake of the fortified food (preventing excessive intakes of the fortificant), and the targeting of age groups in which iron deficiency has been found [33].

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