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Effect of iron-, iodine-, and β-carotene–fortified biscuits on the micronutrient status of primary school children: a randomized controlled trial[1–4]

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ABSTRACT

Background: Deficiencies of iron, iodine, and vitamin A are prevalent worldwide and can affect the mental development and learning ability of schoolchildren.

Objective: The aim of this study was to determine the effect of micronutrient-fortified biscuits on the micronutrient status of primary school children.

Design: Micronutrient status was assessed in 115 children aged 6–11 y before and after consumption of biscuits (fortified with iron, iodine, and β-carotene) for 43 wk over a 12-mo period and was compared with that in a control group (n = 113) who consumed nonfortified biscuits. Cognitive function, growth, and morbidity were assessed as secondary outcomes.

Results: There was a significant between-group treatment effect on serum retinol, serum ferritin, serum iron, transferrin saturation, and urinary iodine (P <0.0001) and in hemoglobin and hematocrit (P <0.05). The prevalence of low serum retinol concentrations (<0.70 μmol/L) decreased from 39.1% to 12.2%, of low serum ferritin concentrations (<20 μg/L) from 27.8% to 13.9%, of anemia (hemoglobin <120 g/L) from 29.6% to 15.6%, and of low urinary iodine concentrations (<100 μg/L) from 97.5% to 5.4%. There was a significant between-group treatment effect (P <0.05) in cognitive function with the digit span forward task (short-term memory). Fewer school days were missed in the intervention than in the control group because of respiratory- (P = 0.097) and diarrhea-related (P = 0.013) illnesses. The intervention had no effect on morbidity and cognitive function.

Conclusions: Fortified biscuits resulted in a significant improvement in the micronutrient status of primary school children from a poor rural community and also appeared to have a favorable effect on anthropometric status. *Am J Clin Nutr* 1999;69:497–503.

KEY WORDS Vitamin A, β-carotene, iron, iodine, fortification, school feeding program, micronutrient deficiencies, intervention, cognitive function, morbidity, primary school children

INTRODUCTION

Deficiencies of iron, iodine, and vitamin A are considered to be a public health problem worldwide (1). According to a national survey in South Africa (2), 33% of children aged <6 y suffer from subclinical vitamin A deficiency (serum retinol <0.70 μmol/L) and 21% from anemia (hemoglobin <110 g/L). Although less is known about the prevalence of iodine deficiency, its occurrence has been reported in certain geographic areas (3, 4) as well as in countries bordering South Africa (5). Goals set for the year 2000 at the World Summit for Children in 1990 include the virtual elimination of vitamin A and iodine deficiencies and the reduction of iron deficiency in women by one-third (1).

Deficiencies of both iron and iodine can affect the mental development and learning ability of schoolchildren. Supplementing anemic children (6, 7) and even nonanemic, iron-deficient children (8) with iron has been shown to have a positive effect on cognitive performance. Iron deficiency can also increase susceptibility to infections (9), which can affect school attendance and achievement. Iodine deficiency can lead to a spectrum of disorders ranging from severe mental retardation to milder forms of motor and cognitive deficits (10). Although damage due to iodine deficiency early in life is usually irreversible, recent studies suggest that there might be an additional component of iodine deficiency that can be reversed (11). Xerophthalmia and childhood blindness are no longer viewed as the only consequences of vitamin A deficiency; milder forms of vitamin A deficiency can impair the immune response (12), which may have an effect on school attendance and consequently performance. Vitamin A deficiency also affects iron metabolism. It has been shown that responses to iron fortification are limited in children with marginal vitamin A status (13) and that supplementation with iron is more effective when iron is given in conjunction with vitamin A (14).

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There are various strategies for addressing micronutrient deficiencies (1). Nutrition education and food diversification offer long-term solutions, but may take decades to show an effect. Supplementation is a short-term solution to acute nutritional deficiencies, whereas food fortification offers a solution in both the medium and long term. For food fortification to be effective, it is important that a suitable vehicle be found. Fortification can be aimed at a population in general or be targeted at specific segments of a population.

In this study we determined the effect of a biscuit fortified with iron, iodine, and β-carotene on the micronutrient status of primary school children living in an area with a known high prevalence of micronutrient deficiencies (15). Because micronutrient deficiencies can also have an effect on cognitive function, growth, and morbidity, these indicators were assessed as secondary outcomes.

SUBJECTS AND METHODS

Study population and design

The study population consisted of children aged 6–11 y in grades 1–5 of the Ndunakazi Primary School, a school in a rural mountainous area ≈ 60 km northwest of Durban, KwaZulu-Natal, South Africa, and serving a community characterized by low socioeconomic status. A cross-sectional nutritional survey of this community revealed a high prevalence of micronutrient deficiencies (15). A dietary intake assessment showed infrequent consumption of animal products; the only β-carotene–rich food consumed regularly was imifino (a dark-green leafy vegetable). All households used salt (noniodized) in the preparation of food; halfway through our study the iodization of salt became compulsory in South Africa, which resulted in the use of only iodized salt during the latter half of the study. A school feeding program in which the children received a cooked meal 5 d/wk had been in operation at the school for 2 y before our baseline assessment. Meals were prepared by a member of the community and usually consisted of soy beans, rice, and vegetables (mostly cabbage and potatoes). This program had, however, been discontinued shortly before the start of our study for reasons unrelated to our intervention and has not resumed. The study was approved by the Ethics Committee of the Medical Research Council and permission was obtained from the Department of Education, the headmaster of the school, and local community leaders. Informed consent was obtained from the parents or guardians of all participants.

The study population was stratified by school grade and the children in each class were then systematically randomly assigned, from alphabetic class lists, to 2 groups. One group received a biscuit fortified with iron, iodine, and β-carotene (n = 126; intervention group), whereas the other group received an unfortified biscuit (n = 126; control group) that was similar to the fortified biscuit in macronutrient composition, taste, and appearance. To enhance the absorption of iron, a vitamin C–fortified cold drink was given to the intervention group; the control group received an unfortified cold drink (placebo). On the basis of a previous iron fortification study in primary school children (16), we calculated that a sample size of 100 would be adequate to show a 3% increase in hemoglobin and a 20% increase in serum ferritin at a 5% significance level with 80% statistical power. The biscuits and cold drinks were distributed daily during the school week during the first 2 h of the school day. No intervention took place during school holidays, weekends, or public holidays; the supplement was provided for a total of 215 d, or 43 wk. Leftover biscuits and cold drinks at the end of the week (as a result of absenteeism) were sent back to the manufacturing company. Micronutrient status was assessed at baseline and 6 and 12 mo after the study began; anthropometric status and cognitive function were assessed at baseline and 12 mo after the study began. Only the project leader was aware of the group allocation (single-blind study). One hundred fifteen children in the intervention group and 113 in the control group completed the study; leaving the area was the main reason for dropping out of the study. To exclude parasitic infestations as a confounding factor, all children were dewormed (with 400 mg albendazole) at 4-mo intervals for the duration of the study; the first treatment took place after blood was drawn at baseline, but before the study began.

Compliance and the reasons for absence from school were monitored closely and recorded daily by nutrition monitors (selected people from the community trained by the research team) on record sheets. To avoid the exchange of biscuits and cold drinks between classmates, the intervention and control groups were seated on opposite sides of the classroom. Distribution and consumption took place under close supervision; children were not allowed to leave the classroom or return to their original seats before they had finished their biscuits and drinks. Information on the acceptability of the biscuits and cold drinks, as well as information on breakfast and snacking patterns during the school day, was obtained by means of a short questionnaire administered at the baseline and 6- and 12-mo assessments.

Fortification

The shortbread-based biscuits (cookies) were designed to provide 50% of the recommended dietary allowances of iron (5 mg ferrous fumarate), iodine (60 μg potassium iodate), and β-carotene (2.1 mg) for children aged 7–10 y (17). The sugar-based cold drink (prepackaged in plastic bags) was to provide ≈90 mg vitamin C. Because it was initially uncertain how the baking process would affect the stability of iodine in the biscuit, 60 μg I was added to the cold drink as well. The compositions of the biscuits and cold drinks are shown in **Table 1**. Shelf life, in terms of micronutrient composition, was ≥3 mo; there were also no organoleptic changes during this period. The estimated cost of fortifying the biscuits and cold drinks was R4.40 (≈US$0.7) per child, per school year, each; the cost of the cold drink included the additional cost of a special packaging material used to prevent the oxidation of vitamin C.

Laboratory measurements

Blood (5 mL) was obtained by venipuncture. A complete blood count was performed with an automated cell counter (STKS; Coulter Electronics, Hialeah, FL). The rest of the blood was processed and stored at −80°C until assayed. Serum ferritin was determined with an immunoradiometric assay (Ferritin MAb Solid Phase Component System; Becton Dickinson and Co, Orangeburg, NY) with an Auto Gamma 500C counting system (United Technologies, Packard, IL). Serum iron and total iron binding capacity were determined spectrophotometrically with an RA-1000 automated system (Technicon, Tarrytown, NY) using a colorimetric method (Fe SYS 1 and Test-Combination Iron-binding Capacity; Boehringer Mannheim, Mannheim, Germany). Transferrin saturation (TS) was calculated by expressing total serum iron as a percentage of total iron binding capacity. Serum retinol was determined by reversed-phase HPLC, based

TABLE 1
Analyzed composition of the biscuits and cold drinks[1]

Nutrient	Biscuits (45 g)[2]		Cold drink (150 mL)	
	Fortified	Unfortified	Fortified	Unfortified
Iron (mg)	5.9 ± [illegible].1	1.2 ± 0.5	—	—
β-Carotene (mg)	2.0 ± 0.6	Trace	—	—
Iodine (μg)	95.4 ± 27.5	32.9 ± 7.2[3]	39.0 ± 5.4	Trace
Vitamin C (mg)	—	—	110 ± 18	Trace

[1] $\bar{x}$ ± SD based on analyses of 9 batches of each type of biscuit (Aspland and James Ltd. Consultant Analysts, United Kingdom) and 5 batches of each type of cold drink (Medical Research Council, Parow, South Africa); the protein, carbohydrate, and fat contents of the biscuits (45 g) were 4.1, 26.9, and 7.7, respectively; the carbohydrate content of the cold drink was 13.7 g; and the energy contents of the biscuit and cold drink were 810 and 230 kJ, respectively.

[2] Three biscuits weighing 15 g each.

[3] From a marine oil used in the baking process.

on the method described by Catignani and Bieri (18). Urine samples were collected and urinary iodine was determined spectrophotometrically by using the Sandell-Kolthoff reaction (19). Stool samples (collected before the first anthelmintic treatment) were preserved with formalin, filtered, and prepared by the formal-ether method for microscopic examination and identification of helminth eggs.

Anthropometry and thyroid size

Weight was measured (with subjects in light clothing) to the nearest 0.05 kg on an electronic load cell scale; height was measured (with subjects shoeless) to the nearest 0.1 cm with a wooden board fitted with a measuring tape, a fixed-foot plate, and a movable head board. Height-for-age and weight-for-age were expressed as z scores with the National Center for Health Statistics median as the reference (20). The birth date of each child was obtained from the school register. All children were examined by a medical practitioner for an enlarged thyroid; thyroid size was classified as not palpable or visible, palpable but not visible, or visible (3).

Cognitive function tests

Cognitive assessments were conducted on all participating children in grades 2–4 (grade 2, n = 51; grade 3, n = 47; grade 4, n = 37); children in grade 1 were too young to perform the tasks and there were too few children in grade 5. Tests were conducted outside the classroom with the child and the test administrator seated at a table under a tree some distance away from the school building. The tests were designed to record speed of processing and capacity of working memory in tasks closely related to the intellectual skills required for schoolwork. The tests, based on guidelines described by Connolly and Grantham-McGregor (21), were designed for use in this particular age group and were not culturally biased. For 5 of the tasks (digit copying, counting letters, canceling letters, reading numbers, and counting backward), the time that it took the child to complete the task was measured with a stopwatch and recorded. For the verbal fluency, writing crosses, digit span forward, and digit span backward tasks, the amount of the task completed in a set time was recorded.

Morbidity

For each day a child was absent, the reason for absence was retrospectively obtained from the mother or child and recorded by the nutrition monitor. Each illness or reason for absence was assigned a specific code. Disorders such as colds, influenza, chest infection, and cough were categorized as respiratory-related illnesses; diarrhea, vomiting, and nausea were categorized as diarrhea-related illnesses. The first 4 wk of the study were regarded as the run-in phase, and morbidity data for this period were not included in the analyses. No data were collected on weekends and holidays.

Statistical analysis

Analyses were performed with the SAS software program (version 6.12; SAS Institute Inc, Cary, NC). Changes from baseline to the end of the 12-mo study for all variables (including cognitive scores) in the intervention group were compared with those in the control group by using the Wilcoxon 2-sample test. The Wilcoxon signed-rank test for paired data was used to compare pre- and postintervention values within each group. The effect of fortification on the prevalences of micronutrient deficiencies was evaluated by using repeated-measures analysis of variance for categorical data. Morbidity data were compared with the chi-square test. Spearman correlation coefficients were used to test for the association between white blood cell counts and serum ferritin or retinol. P values <0.05 were considered statistically significant.

RESULTS

Baseline characteristics of the intervention and control groups are given in **Table 2**. Only a small percentage of the children were stunted and almost none were underweight (< −2 SDs of the National Center for Health Statistics reference median for height-for-age and weight-for-age, respectively). Both vitamin A deficiency and goiter were present at levels regarded as being a public health problem (10, 22). About one-third of the population was infected with at least one parasite (mostly *Trichuris trichiura*: 27% and 25% of the intervention and control groups, respectively).

Mean compliance rate, determined from the record sheets, was 92.4% and 93.4% in the intervention and control groups, respectively; absence from school was the only reason for noncompliance. The taste of both the biscuit and the cold drink was acceptable to all of the children; 74% indicated at the 12-mo assessment that they would prefer more than the 3 biscuits they were

TABLE 2
Baseline characteristics of the study children

	Intervention group (n = 61 M, 54 F)	Control group (n = 57 M, 56 F)
Age (y)	8.8 ± 2.0[1]	8.5 ± 1.9
Height (cm)	125.2 ± 11.4	123.7 ± 10.8
Weight (kg)	26.4 ± 6.3	24.9 ± 5.6
Stunted (%)[2]	14.8 (17 of 115)	9.7 (11 of 113)
Underweight (%)[3]	0 (0 of 115)	3.5 (4 of 113)
Subclinical vitamin A deficiency (%)[4]	39.1 (45 of 115)	40.7 (46 of 113)
Anemia (%)[5]	29.6 (34 of 115)	24.5 (27 of 110)
Goiter (%)[6]	20.0 (23 of 115)	22.1 (25 of 113)
Infected with ≥ 1 parasite (%)	34.3 (34 of 99)	32.7 (33 of 101)

[1] $\bar{x}$ ± SD.

[2] Height-for-age z scores < −2 SDs of the National Center for Health Statistics median (20).

[3] Weight-for-age z scores < −2 SDs of the National Center for Health Statistics median (20).

[4] Serum retinol <0.70 μmol/L.

[5] Hemoglobin <120 g/L.

[6] Visible or palpable.

TABLE 3
Micronutrient status of subjects before (baseline) and 6 and 12 mo after the study began

	Intervention group		Control group	
	n	Median (10th and 90th percentiles)	*n*	Median (10th and 90th percentiles)
Serum retinol (μmol/L)				
Baseline	115	0.74 (0.56, 1.03)	113	0.74 (0.52, 1.01)
6 mo	115	0.84 (0.61, 1.16)[1]	113	0.76 (0.52, 1.02)
12 mo	115	0.87 (0.65, 1.19)[1,2]	113	0.75 (0.54, 1.00)
Serum ferritin (μg/L)				
Baseline	115	29.2 (13.1, 56.7)	113	31.3 (15.9, 73.0)
6 mo	114	34.1 (18.8, 65.9)[3]	111	24.2 (14.2, 55.3)[1]
12 mo	115	33.6 (19.2, 56.9)[2,3]	113	22.7 (12.5, 44.2)[1]
Serum iron (μmol/L)				
Baseline	113	13.1 (4.7, 19.7)	113	12.4 (4.5, 18.9)
6 mo	110	16.9 (6.9, 25.9)[1]	108	14.0 (7.9, 19.1)[4]
12 mo	113	17.4 (10.5, 24.9)[1,2]	113	12.5 (6.5, 18.6)
Transferrin saturation (%)				
Baseline	113	21.4 (7.5, 33.2)	113	19.9 (7.0, 37.6)
6 mo	110	26.8 (11.6, 41.3)[1]	108	21.1 (10.5, 33.1)
12 mo	113	26.1 (15.0, 35.6)[1,2]	113	17.4 (10.7, 25.9)[4]
Hemoglobin (g/L)				
Baseline	115	125 (117, 135)	110	126 (115, 136)
6 mo	115	124 (112, 135)[4]	110	124 (113, 133)[3]
12 mo	115	129 (117, 139)[1,5]	110	127 (115, 136)
Hematocrit				
Baseline	115	0.356 (0.332, 0.388)	110	0.362 (0.331, 0.388)
6 mo	115	0.345 (0.315, 0.377)[1]	110	0.342 (0.316, 0.368)[1]
12 mo	115	0.364 (0.331, 0.396)[1,6]	110	0.362 (0.332, 0.388)
Urinary iodine (μg/L)				
Baseline	108	20 (8, 47)	108	20 (7,68)
6 mo	105	148 (49, 254)[1]	107	35 (12, 108)[1]
12 mo	108	225 (113, 289)[1,2]	108	137 (42, 267)[1]
White blood cell count ($\times 10^9$/L)				
Baseline	115	7.6 (5.2, 11.5)	110	8.2 (5.2, 11.5)
6 mo	115	7.5 (5.3, 11.5)	110	7.1 (5.3, 11.1)[1]
12 mo	115	7.4 (5.3, 11.2)	110	6.9 (4.8, 10.2)[1]

[1,3,4] Significantly different from baseline (Wilcoxon signed-rank test for paired data): [1] $P < 0.0001$, [3] $P < 0.005$, [4] $P < 0.05$.
[2,5,6] Change from baseline significantly different from that for control group (Wilcoxon two-sample test): [2] $P < 0.0001$, [5] $P = 0.0015$, [6] $P = 0.0365$.

receiving. Most of the children (89%, 90%, and 94% at the baseline and 6- and 12-mo assessments, respectively) reported eating breakfast before coming to school; reasons for not eating breakfast were mainly "late for school," "not hungry," or "no food available." Very few children (<5% at all 3 assessments) reported bringing food to school; however, 70% of them reported bringing money to school to buy something to eat during the day. Items usually purchased from the local shop or from fellow students were potato chips (crisps), sweets, cold drinks, cookies, sandwiches, fried fish, and fruit.

Micronutrient status

The micronutrient status of the intervention and control groups before and 6 and 12 mo after the study began is presented in **Table 3**. A significant treatment effect compared with the control group was found for serum retinol, serum ferritin, serum iron, TS, urinary iodine, hemoglobin, and hematocrit. Serum ferritin, serum iron, and TS values, however, appeared to reach a stable median in the intervention group after 6 mo. A decrease in serum ferritin was observed in the control group. In both the intervention and control groups, hemoglobin and hematocrit decreased slightly at 6 mo. Urinary iodine excretion increased significantly in both groups, although the increase in the intervention group was significantly greater than that in the control group.

The prevalence of low micronutrient concentrations before and 6 and 12 mo after the study began is shown in **Figure 1**. The percentage of children with low serum retinol concentrations in the intervention group decreased from 39.1% before the intervention to 12.2% after 12 mo of intervention, while remaining at ≈ 40% in the control group. The percentage of children with low serum ferritin concentrations in the intervention group decreased from 27.8% to 13.9%. In the control group, the percentage increased. The prevalence of anemia decreased from 29.6% to 15.6% in the intervention group and from 24.5% to 19.4% in the control group. More than 95% of children in both groups had a urinary iodine excretion < 100 μg/L at the baseline assessment; this prevalence decreased to 5.4% in the intervention group and to 34.6% in the control group after 12 mo. Repeated-measures analysis of variance for categorical data showed a significant interaction between time and treatment for serum retinol ($P = 0.0002$), serum ferritin ($P = 0.0005$), and urinary iodine ($P < 0.0001$). The prevalence of goiter, which was 20% and 22.1% at the baseline assessment in the intervention and control groups, respectively (19% palpable; 2% visible), did not decrease after 12 mo of iodine fortification.

A weak but significant correlation was found between serum ferritin concentrations and white blood cell counts in the control group at the baseline assessment ($r = 0.24$, $P = 0.0131$), but not

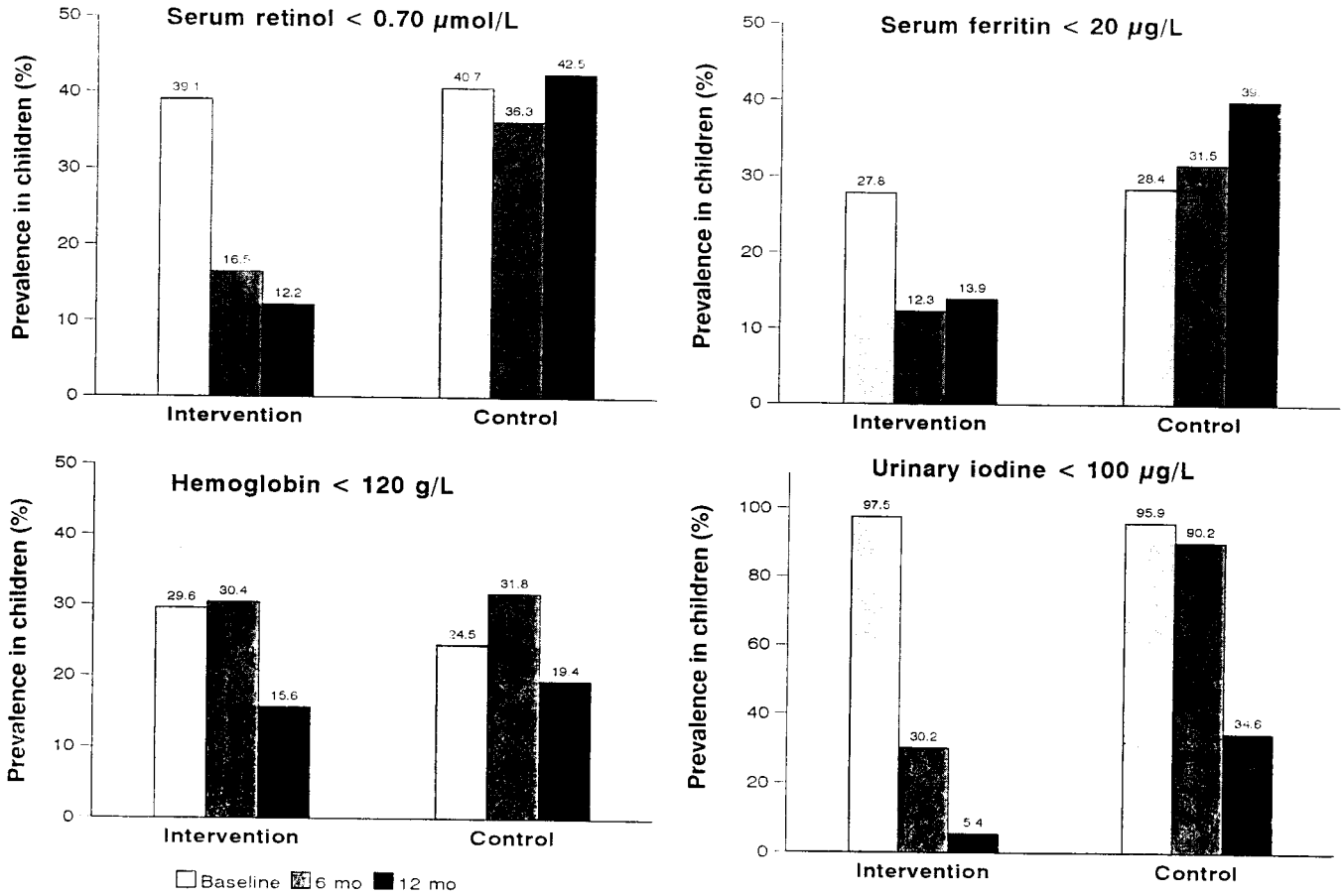

FIGURE 1. Prevalence of low serum retinol, serum ferritin, hemoglobin, and urinary iodine concentrations in subjects at baseline and 6 and 12 mo after consumption of fortified (with iron, iodine, and β-carotene) or nonfortified (control) biscuits. Repeated-measures analysis of variance for categorical data showed a significant interaction between time and treatment for serum retinol ($P = 0.0002$), serum ferritin ($P = 0.0005$), and urinary iodine ($P < 0.0001$)

at the 6- and 12-mo assessments. A decrease in median white blood cell counts was observed over the 12-mo period, which was significant in the control group (Table 3). No correlation was found between serum retinol and white blood cell counts in either group at any of the assessments.

Anthropometric status

There was no significant difference in the change in height and weight or height-for-age and weight-for-age z scores over the 12-mo study period between the intervention and control groups.

Cognitive assessment

Results of the cognitive tests are presented in **Table 4**. A significant between-group treatment effect was found for the digit span forward task. Further analyses of the data showed more and greater treatment effects in the children with low serum ferritin and low hemoglobin concentrations and in those with goiter at baseline. These results will be reported elsewhere.

Morbidity data

Fewer school days (per 100 children) were missed by children in the intervention group than in the control group as a result of respiratory-related illnesses (33 d compared with 47 d, $P = 0.097$) and significantly fewer as a result of diarrhea-related illnesses (52 d compared with 79 d, $P = 0.013$).

DISCUSSION

This study showed that fortification of a biscuit with iron, iodine, and β-carotene resulted in a significant improvement in the micronutrient status of primary school children from a poor rural community. Before our intervention, a feeding program had been in operation at the school for 2 y. Despite this program, a substantial number of children at our baseline assessment had micronutrient deficiencies at the biochemical level, indicating that this feeding program did not supply enough micronutrients to prevent or eliminate existing micronutrient deficiencies.

Our intervention resulted in a drop in the prevalence of low serum retinol concentrations from a level regarded as being a severe public health problem [>20% of a population with serum retinol concentrations <0.70 μmol/L (22)] to one almost no longer regarded a problem. A β-carotene–fortified wafer also resulted in a significant improvement in serum retinol concentrations in lactating women in a study in Indonesia (23). This study showed no improvement in vitamin A status when the same amount of β-carotene was obtained in the form of dark-

TABLE 4
Change in cognitive scores from baseline to 12 mo[1]

Task	Intervention group		Control group	
	Baseline	Change	Baseline	Change
Verbal fluency (number of items)	46.3 ± 8.7 [67]	1.73 ± 9.12	45.7 ± 9.0 [68]	1.68 ± 9.56
Digit copying (time: s)	108.7 ± 35.0 [65]	−21.3 ± 26.2	108.0 ± 34.2 [68]	−22.7 ± 26.2
Writing crosses (number of crosses)	11.3 ± 2.7 [67]	0.97 ± 2.68	11.6 ± 2.4 [68]	1.25 ± 2.21
Counting letters (time: s)	28.1 ± 12.5 [67]	−3.94 ± 14.3	32.2 ± 14.3 [68]	−5.90 ± 15.3
Canceling letters (time: s)	43.7 ± 15.9 [67]	−10.3 ± 14.7	45.5 ± 18.9 [68]	−11.7 ± 16.6
Reading numbers (time: s)	48.5 ± 26.1 [64]	−13.0 ± 21.3	45.8 ± 18.0 [64]	−10.3 ± 11.5
Digit span forward task (number of digits)	4.8 ± 1.0 [67]	0.61 ± 1.01[2]	5.0 ± 0.82 [68]	0.25 ± 0.83
Digit span backward task (number of digits)	3.1 ± 0.8 [62]	0.55 ± 1.26	3.2 ± 1.0 [66]	0.59 ± 1.25
Counting backward (time: s)	63.3 ± 25.0 [47]	−21.5 ± 22.9	66.5 ± 37.2 [43]	−25.5 ± 29.9

[1] $\bar{x}$ ± SD; *n* in brackets.
[2] Significantly different from change in control group, $P = 0.04$ (Wilcoxon two-sample test).

green leafy vegetables. The authors suggest that β-carotene from dark-green leafy vegetables is poorly absorbed because it is trapped in a complex matrix within plant cells. This low bioavailability may also be the reason why 40% of the children in our study had subclinical vitamin A deficiency at the baseline assessment, despite their regular consumption of imifino—a dark-green leafy vegetable providing ≈7 μg retinol equivalents vitamin A/g cooked portion.

Although the prevalence of anemia in both groups combined was 27%, and 32% of the children had low TS values, few children (5.7%) were iron deficient (ferritin < 12 μg/L) and only 3% had both low TS and low ferritin values. It is possible that serum ferritin may have been elevated because of the presence of infections (24), thereby obscuring the real prevalence of iron deficiency. The decrease, for no apparent reason, in serum ferritin from baseline to 12 mo in the control group, as well as the concomitant drop in white blood cell counts, strengthens this possibility. Helminth infections may have contributed to a higher infection rate at baseline because the children were dewormed only after a blood sample had been drawn. C-reactive protein, a more sensitive indicator of infection, was unfortunately not measured. It is difficult to explain the decrease in hemoglobin at 6 mo; a decrease was, however, also experienced in the control group. Seasonal hemodilution, which was described elsewhere (25) and was also observed in a previous study by our group (13), might have played a role. Serum ferritin, serum iron, and TS appear to have reached a plateau after 6 mo of intervention. Absorption of iron is known to be inversely related to the size of body iron stores (9). It is therefore possible that less iron was absorbed as the iron status of the study population improved or that there was a mucosal block to iron absorption resulting from prior iron administration (26). Because we do not have data on the effects of the intervention before 6 mo, it is not known at what stage of the study this plateau was reached.

Median urinary iodine excretion in the intervention group increased significantly from a concentration regarded as a moderate to severe public health problem (severe: <20 μg/L) to a concentration no longer regarded as a public health problem (median: ≥100 μg/L) (10). The slight increase in the control group at 6 mo can be explained by the fact that the unfortified biscuits also contained some iodine, derived from a marine oil used in the baking process. Because the iodization of salt (40–60 ppm) became compulsory in South Africa shortly after our 6-mo assessment had been completed, we had the unique opportunity to use the second half of our study to evaluate the effect of iodized salt on our study population. At 12 mo, the median urinary iodine concentration in the intervention group increased further to >200 μg/L, whereas in the control group it rose to a concentration similar to that observed in the intervention group after the first 6 mo of the study. Consumption of iodized salt was thus as effective as the biscuits in raising urinary iodine concentrations and had the additional benefit of reaching a much wider population. We found no reduction in the prevalence of goiter in either group; 12 mo of fortification might, however, have been too short to reverse an already enlarged thyroid.

The intervention had no effect on anthropometric status. However, few children were stunted or underweight at baseline. The high prevalence of micronutrient deficiencies, despite the low prevalence of stunting and underweight, emphasizes the danger of relying on anthropometric data as the only indicator of nutritional status; the term "hidden hunger," as micronutrient malnutrition is often referred to, appropriately describes the situation in this population before the intervention.

The cognitive tests administered to the children were designed to measure a range of mental processes and fine motor skills (eg, verbal learning, visual memory, arousal, attention, retrieval, eye-hand perception, and coordination) that are thought to be affected by nutritional deficits. A significant improvement was found in the results of the digit span forward task only, which is a measure of short-term memory and attention. Cognitive development can be influenced by factors other than micronutrient deficiencies, eg, parasitic infection (27) and short-term hunger (28). In the present study, both groups received anthelmintic therapy and the confounding effect of short-term hunger was eliminated by the placebo biscuit, which supplied an equivalent amount of macronutrients. A confounding factor beyond our control, however, was the compulsory iodization of salt during the second half of our study. Iodine-related improvements in cognitive function that might have occurred in the intervention group would have been partially masked by improvements in the control group. The best way to have shown the effect of micronutrients on cognitive function would have been to include only children with micronutrient deficiencies because an effect would not have been expected in children who were micronutrient replete. Our study included both micronutrient-deficient and micronutrient-replete children, thus diluting possible intervention effects. Further analyses of our data showed more significant intervention-related effects in those children with low micronutrient statuses at baseline; this data will be reported elsewhere.

Both iron and vitamin A deficiencies can increase susceptibility to infections (9, 12). The fewer school days lost in the intervention group as a result of respiratory- and diarrhea-related illnesses could have beneficial effects on learning should the children receive fortified biscuits for several years as part of a school feeding program. Two shortcomings of our method of morbidity data collection, however, were that morbidity data were not collected for weekends and holidays and that diagnoses were made by nutrition monitors on the basis of information provided by the children's mothers.

We showed that a biscuit can be used successfully as a vehicle for nutrient fortification in school feeding programs. Consumption of the fortified biscuit resulted in a significant improvement in micronutrient status and also appeared to have a favorable effect on the morbidity and cognitive function of the schoolchildren in this community. A major advantage of using biscuits as a fortification vehicle is that it is considered to be a snack rather than a meal and is therefore unlikely to replace meals given to the child at home. Additional advantages are that it needs no preparation, is easy to distribute, has a long shelf life, and can be easily monitored. The cold drink used in the study served merely as a carrier of vitamin C to enhance the absorption of iron. Use of a more bioavailable form of iron as a fortificant, eg, an iron chelate (29), could eliminate the need for vitamin C, and thus the cold drink, reducing the cost of intervention by half.

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