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Zinc supplementation reduced morbidity, but neither zinc nor iron supplementation affected growth or body composition of Mexican preschoolers¹⁻³

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See corresponding editorial on page 160.

ABSTRACT In rural Mexico and in many developing countries micronutrient deficiencies, growth stunting, and morbidity from infectious diseases are highly prevalent in young children. We assessed the extent to which growth stunting could be reversed and the number of infectious disease episodes reduced by zinc and/or iron supplementation. In a double-blind, randomized community trial 219 Mexican preschoolers were supplemented with either 20 mg Zn as zinc methionine, 20 mg Fe as ferrous sulfate, 20 mg Zn + 20 mg Fe, or a placebo. After 12 mo, plasma zinc increased significantly in the two zinc-treated groups, and plasma ferritin was significantly higher in the two iron-treated groups. There was no effect of treatments on growth velocity or body composition. Children in both zinc-supplemented groups had fewer episodes of disease (zinc alone, 3.9 ± 0.3 ; zinc + iron, 3.7 ± 0.4 ; placebo, 4.6 ± 0.5 ; $P < 0.03$), including diarrhea (zinc alone, 0.7 ± 0.1 ; zinc + iron, 0.8 ± 0.1 ; placebo, 1.1 ± 0.2 ; $P < 0.01$). Zinc and zinc + iron supplements reduced morbidity but had no effect on growth or body composition. *Am J Clin Nutr* 1997;65:13-9.

KEY WORDS Zinc, iron, Mexico, supplementation, growth, body composition, morbidity, children

INTRODUCTION

Undernutrition is manifested in most developing countries by early growth stunting and a high prevalence of micronutrient deficiencies. National surveys in Mexico showed that 25-50% of preschool children in rural areas are stunted (1), and that anemia affects 16-51% of urban children and $\leq 91\%$ of those in poorer rural regions (2, 3).

The present study was conducted in the Valley of Solís, a rural region in central Mexico, as a logical intervention based on previous information about the nutritional status of children and adults in the valley. The children have been of normal weight and length when born, but compared with international reference values length Z scores fall immediately after birth, and weight Z scores start to fall at ≈ 3 mo of age (4). This growth faltering continues until 22 mo of age after which time growth rate is comparable with international reference values. Similar growth patterns have been reported in studies in other countries (5-7). The early growth stunting is likely to persist through adolescence if children remain in the same location (8)

but may be at least somewhat reversed if diet and environmental conditions are improved (9, 10).

The causes of early growth stunting are not yet understood (11), but may include a nutritionally inadequate diet as well as clinical (12) or subclinical (13) infections. Although growth stunting has been traditionally attributed to protein-energy malnutrition, it is widespread even where protein and energy intakes are adequate (5, 6, 11) such as in Solís (14). Stunting is associated with habitual consumption of a diet that is low in animal products and accompanying micronutrients, and high in plant constituents such as phytate that inhibit the absorption of minerals (15, 16). We showed previously that the absorption of both zinc and iron is lower from a rural Mexican diet consisting primarily of maize than from a more refined urban Mexican diet (17). Because zinc supplementation has improved the growth and/or body composition of stunted children in countries such as the United States, Canada, Ecuador, China, and Guatemala (11, 18), the present study was designed to measure the effect of zinc supplementation on the growth and body composition of Mexican preschoolers. Unlike most of the previous zinc-supplementation studies reported in the literature, iron supplements were also provided because of the high prevalence of iron deficiency in this community (19). There is some, albeit limited, evidence that iron deficiency causes poor appetite and growth stunting (20), so we were concerned that simultaneous iron deficiency might have limited any zinc-induced growth response.

Both zinc and iron deficiency cause impaired immune response (21, 22), but it remains to be determined whether community-level supplementation with zinc or iron will reduce morbidity in marginally malnourished populations. We

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therefore measured morbidity as an outcome of zinc and iron supplementation and as a potential confounder of the effect of supplementation on growth and body composition.

SUBJECTS AND METHODS

Subjects and location

The study was conducted in five rural communities in the Valley of Solís, located in the central highland plateau of the state of Mexico \approx 150 km northwest of Mexico City. The communities ranged in size from 700 to 1500 individuals, or from \approx 100 to 214 households. A census revealed that 290 children met our eligibility criterion of being between 18 and 36 mo old. The mothers of all of these children were invited to attend a meeting during which they were informed about the study purpose and protocol and potential risks and benefits. The mothers of 219 children attended the meeting, agreed to participate, and signed consent forms. This number of children met our goal of 48 per treatment group (192 total), which would have detected a difference of 1 cm in height with 80% power, assuming the SD of height change would be 1.5.

The protocol was approved by the Committee on Biomedical Research in Human Subjects of the National Institute of Nutrition, Mexico, and the Committee on the Use of Human Subjects in Research at the University of Connecticut.

Zinc and iron supplementation

Children were stratified by age and sex, and ranked by height, then they were randomly assigned to one of four treatment groups within each stratum. Ages were confirmed by birth certificates.

The four groups received a daily supplement consisting of 20 mL of a solution containing either 20 mg elemental Zn as zinc methionine, 20 mg Fe as ferrous sulfate, 20 mg Zn + 20 mg Fe, or a placebo (solution alone). Zinc methionine (Inter Health Co, Concord, CA) was chosen as the zinc source after we showed that it was better absorbed than other sources of zinc (23) and theoretically would reduce the risk of the zinc being bound by dietary phytate in the intestine. Ferrous sulfate was selected because it is the form of iron that is most commonly used for supplementation. Both the zinc and the iron salts were dissolved in a solution to disguise their bad taste and to ensure similar appearance. This solution contained sugar, citric acid, water, and artificial flavor (either orange or lemon). Before the study, the acceptability of the supplements was tested by sensory evaluation in children of the same age. The solutions were coded in such a way that their content was unknown to any of the project personnel, and the code was not broken until the end of data analysis.

Children in each group received the supplements for 12 mo. They were visited in their homes from Monday through Friday by a fieldworker who gave the supplement and ensured that it was completely consumed in her presence. The flavor of the supplement (lemon or orange) was changed every week to improve compliance. Compliance was excellent; the supplements were consumed on average on 97% of the days they were administered. Only 25 children were dropped from the study before the end of the 12 mo, primarily because of a changing family situation. Data from these children were not used in the statistical analyses.

Anthropometry

Anthropometric data were collected at baseline (before supplementation) and within 2 wk after 6 and 12 mo of supplementation. Measurements on all three occasions were performed by the same examiner (PL) following standard procedures (24). Measures included weight to 0.1 kg on a pediatric scale, standing height to 0.1 cm with an anthropometer, midupper arm circumference (MAC) to 0.1 cm by using a fiberglass tape measure on the left arm, and triceps skinfold thickness accurate to 0.1 mm by using a Lange skinfold caliper.

Clinical examinations and morbidity data

A clinical exam was conducted by a physician in the field clinic at baseline and at 6 and 12 mo after supplementation. Data collected during this exam included signs of nutrient deficiencies or other diseases. Any current diseases received appropriate treatment. No clinical symptoms of micronutrient deficiencies were apparent, and no child was dropped from the study on the basis of the relatively minor diseases that were detected.

Morbidity of the preschoolers was evaluated twice weekly by a questionnaire administered by a trained fieldworker who visited each child at home. Information was obtained from the child's mother about the presence or absence of illness on the day of the visit and since the previous visit. Any illness was recorded by the fieldworker on a precoded list that included the most common diseases and their symptoms, as well as the date when the symptoms started and the date when they disappeared. When the fieldworker had any doubt about the diagnosis or course of the disease, the physician in charge of the field clinic visited the child to confirm the diagnosis. Only data on infectious diseases were analyzed, with symptoms classified by a physician into the following categories: upper and lower respiratory disease (combined because there were only four episodes of lower respiratory disease), diarrhea, fever, and "other." "Respiratory disease" was defined as having any symptom such as runny nose, common cold, sore throat, or cough. "Diarrhea" was defined by the mothers based on their observation of frequent, loose stools. In this study and in our previous research in these communities we found a strong association between mothers' reporting and the physician's diagnosis of diarrhea (19). "Fever" was based on maternal reporting.

Biochemical indicators of zinc and iron status, and other nutrient deficiencies

A 2-mL sample of venous blood was collected from every preschooler at baseline and at 6 and 12 mo after supplementation. After the children had fasted overnight, blood samples were collected in an evacuated container and transferred to a tube that contained 0.05 mL sodium citrate as an anticoagulant. Duplicate hemoglobin and hematocrit determinations were performed within 3 h of blood collection. Hemoglobin was determined by using a Coulter counter (Coulter Electronics, Hi-aleah, FL). Plasma and red blood cells were dispensed as aliquots and frozen at -70°C until analyzed. Plasma zinc was determined in duplicate by atomic absorption spectrophotometry, and plasma ferritin was measured by using a solid-phase radioimmunoassay (Coat-A-Count Ferritin IRMA; Diagnostic

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Products, Los Angeles) and an international standard obtained from the World Health Organization International Laboratory for Biological Standards (National Institute of Biological Standards and Control, Hertsfordshire, United Kingdom). To detect infections or inflammation, plasma C-reactive protein (CRP) was measured by a Behring laser nephelometer after adding antiserum for CRP (Behring Diagnostics, Inc, Somerville, NJ); a protein control serum was included in the test (Behring Diagnostics, Inc).

Statistical analysis

All analyses were conducted by using SAS software for microcomputers. Analyses of the differences among the groups, and between each treatment group and the placebo group, were tested by analysis of covariance using initial values as covariates. Z scores were calculated from National Center for Health Statistics (NCHS) reference values for weight and height (25). Midarm fat area (MAFA) and midarm muscle area (MAMA) were derived from MAC and triceps-skinfold-thickness measurements (26). Changes in anthropometric measures were also analyzed separately for children who were stunted [height-for-age Z score (HAZ) < -2.0]. Morbidity data, combined from the entire 12 mo of the study because of the relatively low prevalence of illness, were analyzed by a two-way nonparametric analysis of variance and significant differences among groups were compared by the Kruskal-Wallis test (27). A *P* value < 0.05 was considered significant.

RESULTS

Assessment of growth and body composition

The characteristics of subjects in each group are shown in Table 1. No characteristic differed significantly among treatment groups. The children were growth stunted, with a mean (\pm SEM) HAZ of -1.6 ± 0.8 . However, as expected, their weight-for-height was normal on average, showing that wasting was not a general problem in the group. No sex differences in anthropometry were found initially or in response to treatment, so that data are presented for the sexes combined.

Changes in weight, height, and Z scores after the 12 mo of intervention are shown in Table 2. The average linear growth rate varied from 8.9 to 9.3 cm/y among the treatment groups and was unaffected by type of treatment. In addition, in the

three nutrient-supplemented groups final Z scores for weight-for-age (WAZ) and weight-for-height (WHZ) were similar to those in the placebo group. The growth velocities among treatments for only those children with an initial HAZ < -2.0 are also compared in Table 2. Although the group supplemented with zinc alone had a faster rate of height growth and a larger improvement in HAZ than the other groups, these differences were not significant. Similar results were found when all anthropometric data were analyzed 6 mo after the start of supplementation (not reported). We also analyzed the growth response of children with plasma zinc concentrations < 10.7 $\mu\text{mol/L}$ at baseline, and found it to be unaffected by any treatment.

Changes in indicators of body composition after 12 mo of intervention are shown in Table 3. There were no significant differences among groups in any of the body composition indicators. This lack of treatment effect on body composition persisted when data were analyzed separately for children with an initial HAZ < -2.0 (Table 3), and when data were analyzed after the first 6 mo of intervention or for the group with initial plasma zinc < 10.7 $\mu\text{mol/L}$ (data not shown).

Biochemical responses to supplementation

Changes in hemoglobin and biochemical indicators of nutritional status after 12 mo of intervention are described in Table 4. Both iron-supplemented groups (ie, iron alone, and zinc + iron) responded to supplementation with a highly significant increment in ferritin, whereas there was no increase in ferritin in the placebo- or zinc-supplemented groups. The prevalence of iron deficiency (plasma ferritin < 12 $\mu\text{g/L}$) was 43–57% in the four groups at baseline, falling 12 mo later to 24% and 23% in the placebo and zinc groups, respectively, and to zero in the two iron-supplemented groups. The mean hemoglobin concentration increased in all groups during the 12 mo, regardless of iron supplementation.

Plasma zinc increased significantly in the zinc- and zinc + iron-supplemented groups over the 12 mo, indicating that the supplemental zinc was absorbed. The mean prevalence of low plasma zinc (< 10.7 $\mu\text{mol/L}$) was 20% at baseline for all children combined. After 12 mo of supplementation the prevalence of low zinc concentrations was 27% and 21% in the placebo and iron-supplemented groups, respectively, but fell to 14% in the group supplemented with zinc alone and to 8% after supplementation with both zinc and iron. The children who had

TABLE 1
Characteristics of subjects in the four groups at the beginning of the study¹

	Placebo (n = 55)	Iron (n = 53)	Zinc (n = 54)	Zinc + iron (n = 55)
Age (mo)	28.9 \pm 1.06	27.5 \pm 0.94	28.4 \pm 1.02	28.8 \pm 1.2
Height (cm)	83.1 \pm 0.74	82.8 \pm 0.89	83.2 \pm 0.80	83.9 \pm 0.99
Weight (kg)	11.1 \pm 0.20	10.8 \pm 0.23	11.1 \pm 0.20	11.4 \pm 0.27
MAC (cm)	14.6 \pm 0.12	14.4 \pm 0.15	14.4 \pm 0.22	14.8 \pm 0.16
TST (mm)	11.2 \pm 0.31	10.4 \pm 0.30	10.3 \pm 0.27	11.3 \pm 0.34
HAZ	-1.8 \pm 0.12	-1.6 \pm 0.16	-1.6 \pm 0.14	-1.5 \pm 0.13
WAZ	-1.4 \pm 0.08	-1.6 \pm 0.12	-1.4 \pm 0.12	-1.2 \pm 0.12
WHZ	-0.4 \pm 0.08	-0.7 \pm 0.08	-0.4 \pm 0.08	-0.3 \pm 0.12

¹ $\bar{x} \pm$ SEM. MAC, midupper arm circumference; TST, triceps skinfold thickness; HAZ, height-for-age Z score; WAZ, weight-for-age Z score; WHZ, weight-for-height Z score. Z scores were calculated from National Center for Health Statistics reference values (25).

TABLE 2

Effects of treatments on growth velocity and change in Z scores over 12 mo in subjects in the four groups¹

	Placebo	Iron	Zinc	Zinc + iron
All children ²				
Height (cm/y)	9.1 ± 0.22	9.0 ± 0.19	9.3 ± 0.21	8.9 ± 0.19
Weight (kg/y)	2.4 ± 0.07	2.4 ± 0.07	2.4 ± 0.07	2.3 ± 0.07
HAZ	0.13 ± 0.06	0.02 ± 0.06	0.16 ± 0.05	0.07 ± 0.06
WAZ	0.25 ± 0.05	0.28 ± 0.06	0.26 ± 0.05	0.16 ± 0.06
WHZ	0.29 ± 0.06	0.36 ± 0.06	0.25 ± 0.06	0.19 ± 0.08
Children with initial HAZ < -2.0 ³				
Height (cm/y)	9.2 ± 0.34	9.0 ± 0.28	9.6 ± 0.37	9.1 ± 0.32
Weight (kg/y)	2.3 ± 0.11	2.4 ± 0.11	2.4 ± 0.11	2.1 ± 0.16
HAZ	0.32 ± 0.09	0.19 ± 0.08	0.39 ± 0.09	0.31 ± 0.08
WAZ	0.26 ± 0.08	0.46 ± 0.10	0.38 ± 0.08	0.17 ± 0.14
WHZ	0.16 ± 0.08	0.45 ± 0.09	0.23 ± 0.11	0.03 ± 0.19

¹ $\bar{x} \pm$ SEM. There were no significant differences between groups. MAC, midarm circumference; HAZ, height-for-age Z score; WAZ, weight-for-age Z score; WHZ, weight-for-height Z score.

² $n = 47$ in the placebo, 50 in the iron, 48 in the zinc, and 49 in the zinc + iron group.

³ $n = 19$ in the placebo, 17 in the iron, 18 in the zinc, and 17 in the zinc + iron group.

low plasma zinc after supplementation had values < 9.2 $\mu\text{mol/L}$.

Morbidity response

The effect of supplementation on the number of diarrhea and respiratory disease episodes is shown in Table 5. The total number of disease episodes was substantially lower in both groups supplemented with zinc, although the reduction was significant ($P < 0.05$) only in the group that received iron as well as zinc. Diarrhea episodes were reduced by 37% in the zinc group ($P < 0.05$) and by 28% in the zinc + iron group ($P < 0.05$). Although the differences were not significant, there were fewer total episodes of respiratory disease and fewer episodes per child in both groups supplemented with zinc. When data were combined for both groups who received zinc, compared with the other two groups combined, there was a significant reduction in the total number of episodes of disease (3.8 ± 0.3 compared with 5.0 ± 0.3 , $P < 0.01$) and of diarrhea (0.8 ± 0.1 compared with 1.3 ± 0.2 , $P < 0.01$), but not in the number of episodes of respiratory illness (2.7 ± 0.2 compared with 3.4 ± 0.3) or other disease. None of the supplements reduced the duration of either diarrheal or respiratory disease or

affected the number of episodes of fever. Iron supplementation alone had no effect on any morbidity.

DISCUSSION

Neither zinc nor iron supplementation for 12 mo produced any improvement in the anthropometry of these growth-stunted preschoolers. At baseline the children had a high prevalence of iron deficiency. Iron supplementation produced a significant increase in mean plasma ferritin concentrations and low ferritin values disappeared in the two iron-supplemented groups. There was a spontaneous improvement in hemoglobin in the placebo group, for reasons that are unknown, so that there was no significant effect of the iron supplements on the final hemoglobin concentration. From this and previous studies in these communities (28) it is apparent that hemoglobin synthesis is being limited by multiple micronutrient deficiencies. It is less certain that these children were severely zinc depleted, because their initial mean plasma zinc concentration was > 13.8 $\mu\text{mol/L}$. However, 20% of them had a baseline value < 10.7 $\mu\text{mol/L}$. After 12 mo of supplementation mean plasma zinc

TABLE 3

Changes in body-composition indicators between baseline and 12 mo in the four groups¹

	Placebo	Iron	Zinc	Zinc + iron
All children ²				
MAC (cm)	0.67 ± 0.08	0.73 ± 0.08	0.93 ± 0.02	0.68 ± 0.07
TST (mm)	0.33 ± 0.27	0.46 ± 0.24	0.59 ± 0.30	0.74 ± 0.27
MAMA (cm ²)	1.00 ± 0.18	1.03 ± 0.15	1.20 ± 0.26	0.78 ± 0.16
MAFA (cm ²)	0.57 ± 0.18	0.63 ± 0.16	0.83 ± 0.21	0.76 ± 0.17
Children with initial HAZ < -2.0 ³				
MAC (cm)	0.73 ± 0.15	1.22 ± 0.11	0.94 ± 0.15	0.83 ± 0.14
TST (mm)	0.31 ± 0.31	0.63 ± 0.53	0.82 ± 0.45	0.63 ± 0.50
MAMA (cm ²)	1.25 ± 0.29	1.79 ± 0.25	1.20 ± 0.21	1.07 ± 0.28
MAFA (cm ²)	0.46 ± 0.26	0.97 ± 0.32	0.97 ± 0.31	0.76 ± 0.32

¹ $\bar{x} \pm$ SEM. No means were significantly different from the placebo group. MAC, midarm circumference; TST, triceps skinfold thickness; MAMA, midarm muscle area; MAFA, midarm fat area; HAZ, height-for-age Z score.

² $n = 46$ in the placebo, 46 in the iron, 47 in the zinc, and 47 in the zinc + iron group.

³ $n = 19$ in the placebo, 17 in the iron, 18 in the zinc, and 17 in the zinc + iron group.

TABLE 4

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biochemical indicators between baseline and 12 mo of supplementation in the four groups¹

	Placebo		Iron		Zinc		Zinc + iron	
	0 mo	12 mo	0 mo	12 mo	0 mo	12 mo	0 mo	12 mo
	Plasma zinc (μmol/L)	108 ± 14	118 ± 8	108 ± 13	118 ± 9	109 ± 11	118 ± 7	107 ± 10
Plasma iron (μmol/L)	20.1 ± 44.6	22.9 ± 16.5	21.2 ± 38.1	46.9 ± 24.2 ²	18.9 ± 15.8	19.7 ± 13.5	14.7 ± 15.6	43.6 ± 22.9 ³
Plasma ferritin (μmol/L)	14.2 ± 0.7	14.4 ± 0.6	15.2 ± 0.6	15.2 ± 0.7	13.2 ± 0.6	16.8 ± 0.8 ⁴	16.5 ± 0.6	18.3 ± 0.7 ⁴

SEM. ¹ significantly different from initial value; ² P < 0.05, ³ P < 0.001, ⁴ P < 0.01.

Plasma zinc rose by > 3 μmol/L in the zinc group and by 10 μmol/L in the group supplemented with both zinc and iron. The fact that zinc supplementation reduced morbidity was taken as evidence that initial zinc status was suboptimal in the study sample as a whole.

In a recent meta-analysis of data from zinc intervention trials designed to improve growth, the predictors of length or weight gain response to zinc supplementation were low initial HAZ and low initial plasma zinc concentration, but not the time of supplementation (KH Brown, J Pearson, LH Murphy, unpublished observations, 1996). Several studies have reported a positive effect of zinc on growth in older, but more severely stunted children (11). Thus, one possible explanation for the lack of growth or body composition response to zinc supplementation in these Mexican children is that they were already severely stunted or zinc deficient. Although there was no significant effect of the supplement on growth of those children with an initial HAZ < -2 or with an initial plasma zinc concentration < 10.7 μmol/L, the lack of significance might be due to the small number of these children in each treatment group.

However, the largest difference in height velocity between any of the groups was 0.6 cm among stunted children,

which would have needed a sample size of > 300 children per group to be detected with 80% power. Also, a height difference of 0.6 cm over the course of a year is likely to be unimportant from a practical or functional point of view. Likewise, a sample size of 350 initially stunted children per group would have been needed for the triceps-skinfold-thickness differences to be significant.

Based on previous data from Mexico, it was surprising that only 20% of the children had a plasma zinc concentration < 10.7 μmol/L at baseline. We observed the apparent absorption of zinc from similar maize-based, high-phytate Mexican diets to be < 5% when they were fed to well-nourished adults (17). Using food intake data from children of the same age collected during previous research in this community, Murphy et al (29) calculated their mean zinc intake to be 5.3 mg/d, and predicted that 68% of the children had an inadequate zinc intake, after correction for zinc bioavailability. It is possible that zinc status was protected to some extent by adaptations such as reduced endogenous secretion of the mineral (30). Calculated iron intakes for the same age group averaged 6.8 mg/d. The amount of absorbable iron consumed was predicted

Morbidity of Mexican children during 12 mo of supplementation in the four groups¹

Morbidity measure	Placebo (n = 56)	Iron (n = 54)	Zinc (n = 54)	Zinc + iron (n = 55)
Total disease episodes (n)	255	285	211	202 ¹
Respiratory	179	192	163	139
Diarrheal	62	76	40 ¹	46 ¹
Fever	14	17	8	17
Disease episodes per child (n)				
All episodes ²	4.6 ± 0.5 ³	5.4 ± 0.5	3.9 ± 0.3	3.7 ± 0.4
Respiratory	3.2 ± 0.4	3.6 ± 0.4	3.0 ± 0.3	2.5 ± 0.3
Diarrheal	1.1 ± 0.2	1.4 ± 0.2	0.7 ± 0.1	0.8 ± 0.1
Fever	0.3 ± 0.08	0.3 ± 0.04	0.1 ± 0.06	0.3 ± 0.09
Disease episodes per episode (n)				
All episodes ²	142	162	113	106
Respiratory	9.9 ± 0.5	9.8 ± 0.5	9.4 ± 0.5	9.4 ± 0.6
Diarrheal (d) ³	5.0 ± 0.6	4.3 ± 0.6	4.4 ± 0.4	6.0 ± 1.0
Fever (d)	10.1 ± 1.5	12.5 ± 2.4	11.0 ± 1.6	14.1 ± 2.9
Disease episodes per child with fever (n)				
All disease episodes ²	235	276	190	191
With fever ⁴	48 [20]	60 [22]	43 [23]	53 [28]

¹ significantly different from placebo group, P < 0.05. ² significantly reduced in the zinc-supplemented groups; ³ P < 0.035, ⁴ P < 0.01.

³ calculated because of missing information on disease duration and fever. ⁴ in brackets.

to be inadequate to prevent anemia in 43% of the children, or to provide adequate iron stores for 88% of them (29).

Another possible reason for the lack of an effect of zinc on linear growth in our study could be the coexistence of other micronutrient deficiencies that could be limiting growth. At baseline, 64% of these children had deficient plasma α -tocopherol concentrations (< 5 mg/L), 24% had low (< 200 μ g/L), and 5% had deficient (< 100 μ g/L) plasma retinol concentrations, 33% had low (< 200 ng/L) and 10% had deficient (< 300 ng/L) plasma vitamin B-12 concentrations, and 5% had deficient and 28% had low riboflavin intakes based on the erythrocyte glutathione reductase activity coefficient (unpublished observations). There has been little systematic study of how these or other micronutrient deficiencies might limit the growth of young children (11, 31).

Most studies have reported no evidence for an effect of iron supplementation on the growth of anemic or iron-deficient children (11). Exceptions include the work of Angeles et al (20), who showed a positive effect of iron (30 mg/d) and ascorbic acid (20 mg/d) supplementation on linear growth of anemic Indonesian children compared with a supplement of ascorbic acid alone. The effect was attributed to a reduction in the episodes of respiratory infections and diarrhea observed with iron supplementation. Lawless et al (32) showed a significant increase in appetite and growth when anemic primary schoolchildren in Kenya were supplemented with 30 mg Fe/d for 14 wk. We conclude that iron supplementation did not affect the growth or body composition of these Mexican children, even though there was a high prevalence of iron deficiency before supplementation, the duration of the intervention was long, and the iron deficiency was corrected.

Zinc supplementation reduced the number of morbid episodes in these growth-stunted rural Mexican preschoolers. Specifically, those who received a zinc supplement for 12 mo, either as zinc alone or zinc + iron, had significantly fewer episodes of disease and diarrhea compared with children who received the placebo or iron alone. Zinc is important for the integrity of the immune system (21), and supplements have improved the immunocompetence of malnourished children (33, 34). Both severe and mild zinc deficiency can contribute to the duration and severity of existing diarrheal disease (35, 36). In addition, zinc supplementation of infants with acute and persistent diarrhea was shown in one study to improve mucosal integrity (37). Future studies should investigate the mechanism by which zinc reduces the number of morbid episodes. Diarrhea has been shown in other studies to be associated with stunting, malabsorption and excessive excretion of nutrients, and childhood mortality. Thus, if the results of the present study are confirmed, improving the zinc status of growth-stunted, marginally zinc-deficient children might prove to be an important public health strategy. Because providing iron in addition to zinc did not affect growth or morbidity in this study, and iron and zinc deficiency are likely to occur simultaneously in populations whose diets are high in phytate and/or low in animal products, it is logical to provide iron as well as zinc supplements in regions where iron deficiency is endemic. ■

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