Short-term supplementation with zinc and vitamin A has no significant effect on the growth of undernourished Bangladeshi children[1–3]

Mohammad M Rahman, Fahmida Tofail, Mohammad A Wahed, George J Fuchs, Abdullah H Baqui, and Jose O Alvarez

ABSTRACT

Background: Several vitamin A supplementation trials have failed to improve the growth rate in children. Addition of zinc to vitamin A might result in enhanced growth.

Objective: This study evaluated the effect on growth in children of simultaneous supplementation with zinc and vitamin A.

Design: This was a randomized, double-blind, placebo-controlled intervention trial. Six hundred fifty-three children aged 12–35 mo were randomly assigned to 1 of 4 intervention groups: 20 mg Zn/d for 14 d (Z group), 60 000 retinol equivalents (200 000 IU) vitamin A on day 14 (A group), zinc plus vitamin A (ZA group), or placebo syrup and placebo capsule (placebo group). Weight and length were measured at enrollment and again after 3 and 6 mo.

Results: Gains in weight and length during the 6-mo follow-up period were not significantly different among the 4 groups by analysis of variance. Catch-up growth also did not differ significantly among the groups. The proportions of children whose weight-for-age *z* scores did not change or decreased were 57% in the Z group, 46% in the A group, 50% in the ZA group, and 54% in the placebo group (NS). The proportions of children whose length-for-age *z* scores did not change or decreased were 42% in the Z group, 48% in the A group, 53% in the ZA group, and 46% in the placebo group (NS).

Conclusion: Combined short-term zinc supplementation and a single dose of vitamin A has no significant effects on weight and length increments in children over a 6-mo period. *Am J Clin Nutr* 2002;75:87–91.

KEY WORDS Zinc, vitamin A, weight, length, catch-up growth, children, supplementation trial, Bangladesh

INTRODUCTION

Zinc deficiency is associated with growth retardation (1). The results of zinc supplementation trials in children, however, are inconsistent. Some studies documented that zinc supplementation positively affects growth (2–5), whereas others did not (6–8). Some studies showed a positive effect on growth only in male children (4, 9), others showed an effect of zinc supplementation only on weight gain, and still others showed an effect only on height gain (10).

Most vitamin A supplementation trials have failed to show a positive effect of vitamin A on growth in children (11–14). In a review, Allen (15) suggested that it is not a single nutrient that limits a child's growth potential but rather a combination of several macro- and micronutrients that act as limiting factors for growth in children.

Several experimental studies have also shown that vitamin A supplementation fails to improve retinol concentrations in zinc-deficient animals. In contrast, zinc supplementation alone or in combination with vitamin A was shown to increase serum retinol concentrations (16–18). The mechanism for this effect is related to the ability of zinc to synthesize retinol binding protein (RBP), which is essential for the transport of vitamin A (19, 20). Human studies have shown that vitamin A administration to cirrhotic patients with impaired dark adaptation (an increase in vision restoration time in dark light) failed to improve the condition. However, when these patients were supplemented with zinc, their vision restoration time improved (21, 22), indicating that zinc is a limiting factor influencing the efficacy of vitamin A.

Our earlier report from Bangladesh showed that >60% of vitamin A–deficient children remain vitamin A deficient despite supplementation with 3 large doses [15 000 retinol equivalents (RE), or 50 000 IU] of vitamin A at monthly intervals (23). This finding suggests that vitamin A may not be the only limiting factor in these children. Because of the high prevalence of protein-energy malnutrition in Bangladesh, it is conceivable that children in Bangladesh are also deficient in other micronutrients, such as zinc. Addition of zinc to vitamin A may be beneficial in overcoming the failure of periodic, large vitamin A doses. Thus, in the present study we examined whether simultaneous zinc and vitamin A supplementation increases the growth rate in malnourished Bangladeshi children.

[1] From the International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh; the Department of Epidemiology & International Health, the School of Public Health, University of Alabama at Birmingham; and the Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Stanford, CA.

[2] Supported by the Thrasher Research Fund.

[3] Address reprint requests to MM Rahman, Data Management and Statistics, Public Health Department, County of Santa Clara, 3003 Moorpark Avenue, San Jose, CA 95128. E-mail: mujib_99@yahoo.com.

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SUBJECTS AND METHODS

Study population and sample

This study was conducted in urban slums in the older part of Dhaka City, the capital of Bangladesh. These slums were clusters of households with very high housing density and overall poor facilities (lacking an adequate water source, garbage removal, paved streets, street lighting, and gas supply). Most of the households (>90%) were constructed of poor, nondurable materials, and 82% had only one small room. One-third of the households had access to supplies of cooking gas, but these were usually shared. About two-thirds of the households had electricity and almost all households had access to safe drinking water through either pipes or tube wells. Most of the latrines (92%) were shared among multiple households and were often unhygienic (24).

Children aged 12–35 mo of either sex who had not received any vitamin A supplementation within the past 4 mo were included in the study. However, children with severe malnutrition (weight-for-age <60% of the National Center for Health Statistics median), with signs or symptoms of vitamin A or zinc deficiency, or with any systemic illness such as diarrhea, respiratory infection, fever, or any other illness that warranted medical intervention at the time of enrollment were excluded. Informed consent was obtained from the parents for their children to participate in the study. The study was approved by the Ethical Review Committee of the International Centre for Diarrhoeal Disease Research, Bangladesh, and the Committee of Human Research, The University of Alabama at Birmingham.

Study design, randomization, and supplementation

This was a randomized, double-blind, placebo-controlled trial. Children were randomly assigned to receive either zinc (Z group), vitamin A (A group), zinc plus vitamin A (ZA group), or placebo. The Z group received 5 mL (1 tsp) zinc syrup containing 20 mg elemental Zn/d for 14 d and a placebo capsule on day 14. The A group received 5 mL placebo syrup/d for 14 d and a 60 000-RE (200 000-IU; 60-mg) vitamin A capsule on day 14. The ZA group received 5 mL (1 tsp) zinc syrup containing 20 mg elemental Zn/d for 14 d and a 60 000-RE vitamin A capsule on day 14. The placebo group received 5 mL placebo syrup/d for 14 d and a placebo capsule on day 14.

A local pharmaceutical company (ACME Laboratories Ltd, Dhaka, Bangladesh) prepared the study syrups (zinc and placebo), which were supplied in identical 50-mL bottles. Each 50 mL placebo syrup contained 25 g sucrose, 5 g sorbitol, 50 mg methyl hydroxy benzoate, 15 mg propyl hydroxy benzoate, 5 mg lemon yellow color, 0.1 mL orange flavor, and 50 mL water. The zinc syrup contained all of the above plus 555.77 mg Zn as zinc sulfate (equivalent to 200 mg elemental Zn).

F Hoffmann-La Roche Ltd (Basel, Switzerland) manufactured and supplied the vitamin A and placebo capsules. The vitamin A capsules contained 60 mg (60 000 RE) vitamin A as retinyl palmitate and 26.8 mg α-tocopherol equivalents (α-TE), or 40 IU, vitamin E (as *all-rac*-α-tocopherol), with soybean oil as an excipient. The placebo capsule contained 26.8 mg α-TE vitamin E (as *all-rac*-α-tocopherol), with soybean oil as an excipient. The vitamin A and placebo capsules looked identical. The quality of the vitamin A capsules and zinc syrup was verified by analyzing the retinol and zinc contents of each in the biochemistry laboratory of the International Centre for Diarrhoeal Disease Research, Bangladesh.

The children were randomly assigned by a person not involved in the study who used permuted blocks of random numbers. Sets of 2 bottles and 1 capsule for each child were serially numbered according to the randomization list and corresponding to the study serial numbers.

Sample size

The sample size was based on several outcome measures, including biochemical indexes of vitamin A nutrition status (serum retinol and RBP), diarrhea and acute respiratory infection morbidity, and growth (weight and length gains). The calculated sample size for growth was 400; however, the required sample size was 800 for diarrheal morbidity. Therefore, we recruited 800 children into the study (200 in each group). Eighty-five children (16 in the zinc group, 31 in the A group, 14 in the ZA group, and 24 in the placebo group) were excluded from the study because they received an extra dose of vitamin A (a 60 000-RE capsule) through the Bangladesh "National Vitamin A Week" campaign. Forty-nine (6%) children were subsequently lost to follow-up. Weight and length measurements at 6 mo were missing for 13 children. There were more dropouts from the vitamin A group than from the other groups; however, the baseline characteristics of the children who dropped out of the vitamin A group were not significantly different from those of the children who dropped out of the other groups. Also, the baseline characteristics of the excluded children were not significantly different from those of the children who continued the study (n = 653). Because weight and length were not measured at 3 and 6 mo for the children who dropped out of the study, we could not analyze the data including these children in an intent-to-treat manner. The effect of zinc and vitamin A supplementation on biochemical nutritional indexes is reported elsewhere (25).

Supplementation procedure

At enrollment, a health assistant fed the child 5 mL (1 tsp) syrup from the numbered bottle that corresponded to the randomization list and showed the child's mother how to administer the medicines at home. The mother was given one bottle containing 50 mL (10 tsp) syrup and was instructed to feed her child one spoonful of syrup each morning after breakfast. Also, the mother was instructed to save the bottle after the syrup was finished and to request a replacement if the bottle was broken or lost. After 7 d, the health assistant visited each child at home and calculated the total amount of syrup given by subtracting the amount left over from 50 mL. Each mother was asked whether she had encountered any problems when feeding the syrup (eg, whether the child liked the syrup or vomited) and was then given another 50-mL bottle of syrup. On day 14, the health assistant again visited each child at home and calculated the amount of syrup given. Mothers were asked about any problems encountered while feeding the syrup. Then the health assistant fed the child a vitamin A or placebo capsule.

Blood sampling and anthropometric measurements

Venous blood (3 mL) was collected at enrollment from the first 411 children and on day 21 from 339 children for the measurement of serum retinol (26), RBP (27), C-reactive protein (27), and zinc (28).

Weight was measured at enrollment and once per month for 6 mo. Supine length was measured at enrollment and again after

TABLE 1
Baseline characteristics of the study children[1]

	Z group (n = 165)	A group (n = 157)	ZA group (n = 171)	Placebo group (n = 160)
Age (mo)	23.8 ± 7.0[2]	24.1 ± 7.4	23.4 ± 7.5	23.5 ± 7.3
11–23 mo [n (%)]	80 (48.5)	66 (42.0)	87 (50.9)	82 (51.3)
24–35 mo [n (%)]	85 (51.5)	91 (58.0)	84 (49.1)	78 (48.7)
Male sex [n (%)]	90 (54.5)	87 (55.4)	95 (55.6)	74 (46.3)
Breast-feeding continued [n (%)]	116 (70.3)	104 (66.2)	128 (74.9)	112 (70.0)
Body weight at admission (kg)	9.17 ± 1.48	9.25 ± 1.54	9.05 ± 1.54	9.17 ± 1.62
Mother's education: illiterate [n (%)]	104 (63.0)	100 (63.7)	110 (64.3)	97 (60.6)
Income ($/mo)	63 (17–295)[3]	63 (25–253)	63 (21–232)	63 (11–295)
<50 $/mo [$n$ (%)]	41 (24.8)	40 (25.5)	41 (24.0)	41 (25.6)
50–100 $/mo [$n$ (%)]	98 (59.4)	88 (56.0)	103 (60.2)	92 (57.5)
>100 $/mo [$n$ (%)]	26 (15.8)	29 (18.5)	27 (15.8)	27 (16.9)

[1] Z group, received 20 mg Zn/d for 14 d; A group, received 60 000 retinol equivalents (200 000 IU) vitamin A on day 14; ZA group, received both zinc and vitamin A. There were no significant differences between groups.
[2] $\bar{x}$ ± SD.
[3] Median; range in parentheses.

3 and 6 mo. Children were dressed in light clothing while weighed with use of a balance with a precision of 10 g (Seca, Hamburg, Germany). Length was measured with a locally constructed length board with a precision of 0.1 cm (29).

Data analysis

Data were analyzed with use of the SPSS for WINDOWS (version 8.0; SPSS Inc, Chicago) statistical package. The anthropometric calculations (weight-for-age, weight-for-length, and length-for-age z scores) were done by using the National Center for Health Statistics package (version 3.0; Centers for Disease Control and Prevention, Atlanta). Weight gain was calculated by subtracting initial weight from final weight and was expressed as g·kg initial body wt^{-1}·mo^{-1} (by multiplying by 1000 and dividing by initial body weight in kg and number of months). Length gain was calculated by subtracting initial length from final length and was expressed as cm·100 cm initial length^{-1}·mo^{-1}. Data were cleaned by visual and logical checks and were analyzed by using the SPSS for WINDOWS package. Initially, descriptive statistics were analyzed. Then, means and median values were compared within and between groups. Student's t tests were done for normally distributed data and Mann-Whitney U tests for skewed data. Chi-square tests were performed to compare categorical variables. A two-factor repeated-measures analysis of variance (ANOVA) with interaction was performed on serum zinc, retinol, and RBP data from days 1 and 21. An analysis of covariance (ANCOVA) was done on changes in nutritional status with day 1 as the covariate. Bonferroni corrections were done to adjust for multiple comparisons. Statistical significance was accepted at a probability level of 0.05 (two-tailed).

RESULTS

Six hundred fifty-three children were included in the final analysis: 165 in the Z group, 157 in the A group, 171 in the ZA group, and 160 in the placebo group. The baseline characteristics of the children, such as age, admission body weight, mother's literacy, and family income, did not differ significantly among groups (**Table 1**). Sixty-two percent of the children were stunted (length-for-age < −2.0 z scores) and 67% were underweight (weight-for-age < −2.0 z scores).

Weight and length gains are shown in **Table 2**. Neither weight gain nor length gain differed significantly among groups [by ANOVA, adjusted for age, sex, and nutritional status (baseline weight-for-length)]. Weight and length gains were also compared among groups in male and female children separately (data not shown). Among male children, weight gain (g·kg initial body wt^{-1}·mo^{-1}) was 13.44 ± 9.7 (n = 90) in the Z group, 15.59 ± 8.2 (n = 87) in the A group, 14.91 ± 9.8 (n = 95) in the ZA group, and 15.95 ± 8.8 (n = 74) in the placebo group (NS).

TABLE 2
Weight and length gains during the 6-mo follow-up period[1]

	Z group (n = 165)	A group (n = 157)	ZA group (n = 171)	Placebo group (n = 160)
Weight gain during first 3 mo (g)	581 ± 396	600 ± 413	593 ± 359	595 ± 385
Weight gain during 6 mo (g)	747 ± 485	835 ± 435	801 ± 492	781 ± 461
Weight gain (g·kg^{-1}·mo^{-1})	14.1 ± 9.80	15.5 ± 8.10	15.4 ± 9.90	14.5 ± 9.30
Length gain during first 3 mo (cm)	2.10 ± 1.24	2.18 ± 1.14	2.02 ± 1.60	2.21 ± 1.26
Length gain during 6 mo (cm)	4.29 ± 1.54	4.33 ± 1.41	4.12 ± 1.29	4.25 ± 1.40
Length gain (cm·100 cm^{-1}·mo^{-1})	0.93 ± 0.36	0.94 ± 0.35	0.90 ± 0.31	0.92 ± 0.32

[1] $\bar{x}$ ± SD. Z group, received 20 mg Zn/d for 14 d; A group, received 60 000 retinol equivalents (200 000 IU) vitamin A on day 14; ZA group, received both zinc and vitamin A. There were no significant differences between groups (by ANOVA adjusted for age, sex, and baseline weight-for-length).

TABLE 3
Changes in weight-for-age, weight-for-length, and length-for-age *z* scores during the 6-mo follow-up period[1]

	Z group (n = 165)	A group (n = 157)	ZA group (n = 171)	Placebo group (n = 160)
Weight-for-age *z* score				
Day 1	−2.35 ± 0.90	−2.38 ± 0.92	−2.46 ± 0.84	−2.36 ± 0.91
3 mo	−2.25 ± 0.89	−2.20 ± 0.95	−2.32 ± 0.84	−2.19 ± 0.89
6 mo	−2.37 ± 0.82	−2.31 ± 0.88	−2.44 ± 0.84	−2.37 ± 0.88
Change	−0.03 ± 0.37	0.04 ± 0.33	0.02 ± 0.37	−0.03 ± 0.35
Weight-for-length *z* score				
Day 1	−1.16 ± 0.79	−1.24 ± 0.76	−1.22 ± 0.75	−1.20 ± 0.77
3 mo	−1.04 ± 0.74	−1.10 ± 0.73	−1.08 ± 0.71	−1.08 ± 0.76
6 mo	−1.31 ± 0.76	−1.31 ± 0.67	−1.32 ± 0.73	−1.32 ± 0.78
Change	−0.16 ± 0.59	−0.09 ± 0.53	−0.09 ± 0.58	−0.13 ± 0.57
Length-for-age *z* score				
Day 1	−2.44 ± 1.15	−2.31 ± 1.25	−2.51 ± 1.13	−2.38 ± 1.231
3 mo	−2.42 ± 1.16	−2.30 ± 1.16	−2.52 ± 1.12	−2.31 ± 1.18
6 mo	−2.31 ± 1.10	−2.24 ± 1.16	−2.47 ± 1.10	−2.30 ± 1.20
Change	0.10 ± 0.51	0.05 ± 0.47	0.02 ± 0.49	0.06 ± 0.50

[1] $\bar{x}$ ± SD. Z group, received 20 mg Zn/d for 14 d; A group, received 60 000 retinol equivalents (200 000 IU) vitamin A on day 14; ZA group, received both zinc and vitamin A. There were no significant differences between groups (by ANCOVA with day 1 as the covariate).

The length gains (cm·100 cm initial length^{-1}·mo^{-1}) were 0.949 ± 0.32, 0.932 ± 0.32, 0.902 ± 0.33, and 0.937 ± 0.29 in the Z, A, ZA, and placebo groups, respectively (NS). Among female children, weight gain (g·kg initial body wt^{-1}·mo^{-1}) was 14.95 ± 9.8 (n = 75) in the Z group, 15.33 ± 8.1 (n = 70) in the A group, 16.05 ± 10.2 (n = 76) in the ZA group, and 13.33 ± 9.8 (n = 86) in the placebo group (NS). The length gains (cm·100 cm initial length^{-1}·mo^{-1}) were 0.910 ± 0.38, 0.941 ± 0.38, 0.898 ± 0.28, and 0.910 ± 0.34 in the Z, A, ZA, and placebo groups, respectively (NS).

The changes in *z* scores suggest that there was little catch-up growth in any of the 4 groups (**Table 3**). Weight-for-age *z* score gains were negative in the Z and placebo groups and slightly positive in the A and ZA groups. However, the group means did not differ significantly. The weight-for-length changes were negative in all groups (NS). There was a slight positive gain in length-for-age *z* score in all groups (NS). The proportions of children who had a *z* score gain suggesting catch-up growth were not significantly different in the 4 groups (**Table 4**).

DISCUSSION

The present study showed that addition of zinc to vitamin A supplementation did not increase the growth velocity in mildly to moderately malnourished Bangladeshi children over a 6-mo follow-up period. Another study in this cohort of children showed that vitamin A status improves with combined zinc and vitamin A supplementation (25). Thus, despite an increase in biochemical nutritional indexes with combined zinc and vitamin A supplementation, growth velocity does not increase.

One possible explanation for the lack of a significant effect of zinc and vitamin A supplementation on children's growth in the present study could be the coexistence of additional micronutrient deficiencies, such as of α-tocopherol, vitamin B-12, riboflavin, or vitamin C (15). In the present study, supplementation had no significant effect in either the stunted or the wasted groups. However, weight and length gains in the stunted and wasted children were comparable with those in their well-nourished counterparts, regardless of supplementation status (data not shown). This suggests that deficiencies in other nutrients associated with protein-energy malnutrition may have limited the growth potential in our children. In addition to micronutrients, adequate macronutrient (protein, fat, carbohydrate, and energy) intake is also necessary for growth in children. We did not assess the exact dietary intake of these children.

In most of the studies that reported a beneficial effect of zinc on growth, the duration of supplementation was much longer than in the present study. We supplemented the children with zinc for only 14 d, which probably explains the lack of effect of zinc on growth in our study. Also, zinc supplementation was shown to improve growth in severely stunted children (30). Children in the present study had an average length-for-age *z* score at the beginning of the study of –2.31 to –2.51. We cannot rule out the possibility that a longer supplementation period would have had a different result. Nonetheless, zinc status improved in the Z group and the bioavailability of vitamin A increased significantly in the ZA group. The effect of zinc on growth is mediated

TABLE 4
Proportion of children who showed catch-up growth (increase in *z* scores)[1]

Increase in *z* score	Z group (n = 165)	A group (n = 157)	ZA group (n = 171)	Placebo group (n = 160)
		n (%)		
Weight-for-age				
≤0.0	94 (57.0)	72 (45.9)	86 (50.3)	86 (53.75)
0.01–0.5	56 (33.9)	72 (45.9)	65 (38.0)	62 (38.75)
>0.5	15 (9.1)	13 (8.2)	20 (11.7)	12 (7.50)
Length-for-age				
≤0.0	69 (41.8)	75 (47.8)	90 (52.6)	73 (45.60)
0.01–0.5	65 (39.4)	61 (38.8)	56 (32.8)	57 (35.60)
>0.5	31 (18.8)	21 (13.4)	25 (14.6)	30 (18.80)
Weight-for-length				
≤0.0	104 (63.0)	89 (56.7)	99 (57.9)	87 (54.40)
0.01–0.5	41 (24.8)	48 (30.6)	49 (28.7)	55 (34.40)
>0.5	20 (12.2)	20 (12.7)	23 (13.4)	18 (11.20)

[1] Z group, received 20 mg Zn/d for 14 d; A group, received 60 000 retinol equivalents (200 000 IU) vitamin A on day 14; ZA group, received both zinc and vitamin A. There were no significant differences between groups.

through the synthesis of protein and insulin-like growth factor (3). Vitamin A acts in a hormone-responsive manner by up-regulating the immune system, reducing morbidity, and ultimately exerting an effect on growth. Therefore, the period of supplementation in our study may have been inadequate for modulating such complex mechanisms as the synthesis of protein and other factors that contribute to growth. Furthermore, because the rate of infection was high in this population, zinc stores were depleted rapidly after supplementation.

A large supplementation trial in Ghana showed that large-dose vitamin A supplementation fails to improve growth in children, although the vitamin A significantly reduces mortality and severe morbidity (12). Similarly, vitamin A supplementation did not lead to an increased growth in Chinese children, although a significant reduction in the incidence and severity of diarrhea and respiratory illnesses was noted (13). Our findings are consistent with the results of these studies. Addition of zinc to vitamin A supplementation could not overcome the failure of vitamin A to increase growth velocity.

In conclusion, 14 d of zinc supplementation and single-dose vitamin A supplementation, either alone or in combination, failed to improve the growth velocity of this group of malnourished Bangladeshi children. This finding does not mean that zinc and vitamin A supplementation is not beneficial; rather, it indicates that, in addition to insufficient intakes of zinc and vitamin A, deficiencies of other important micronutrients and an inadequate energy intake may be limiting normal growth in these children.

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REFERENCES

1. Halstead JA, Ronaghy HA, Abadi P, et al. Zinc deficiency in man. Am J Med 1972;53:277–84.
2. Nakamura T, Nishiyama S, Futagoishi-Suginohara Y, Matsuda I, Higashi A. Mild to moderate zinc deficiency in short children: effect of zinc supplementation on linear growth velocity. J Pediatrics 1993; 123:65–9.
3. Ninh NX, Thissen JP, Collette L, Gerard G, Khoi HH, Ketelslegers JM. Zinc supplementation increases growth and circulating insulin-like growth factor I (IGF-I) in growth-retarded Vietnamese children. Am J Clin Nutr 1996;63:514–9.
4. Walravens PA, Chakar A, Mokni R, Denise J, Lemonnier D. Zinc supplements in breastfed infants. Lancet 1992;340:683–5.
5. Walravens PA, Krebs NF, Hambidge KM. Linear growth of low income preschool children receiving a zinc supplement. Am J Clin Nutr 1983;38:195–201.
6. Bates CJ, Evans PH, Dardenne M, et al. A trial of zinc supplementation in young rural Gambian children. Br J Nutr 1993;69:243–55.
7. Meeks Gardner J, Witter MM, Ramdath DD. Zinc supplementation: effects on the growth and morbidity of undernourished Jamaican children. Eur J Clin Nutr 1998;52:34–9.
8. Rosado JL, Lopez P, Munoz E, Martinez H, Allen LH. Zinc supplementation reduced morbidity, but neither zinc nor iron supplementation affected growth or body composition of Mexican preschoolers. Am J Clin Nutr 1997;65:13–9.
9. Castillo-Duran C, Garcia H, Venegas P, et al. Zinc supplementation increases growth velocity of male children and adolescents with short stature. Acta Paediatr 1994;83:833–7.
10. Schlesinger L, Arevalo M, Arredondo S, Diaz M, Lönnerdal B, Stekel A. Effect of a zinc-fortified formula on immunocompetence and growth of malnourished infants. Am J Clin Nutr 1992;56:491–8.
11. Fawzi WW, Herrera MG, Willett WC, Nestel P, el Amin A, Mohamed KA. The effect of vitamin A supplementation on the growth of preschool children in the Sudan. Am J Public Health 1997;87:1359–62.
12. Kirkwood BR, Ross DA, Arthur P, et al. Effect of vitamin A supplementation on the growth of young children in northern Ghana. Am J Clin Nutr 1996;63:773–81.
13. Lie C, Ying C, Wang EL, Brun T, Geissler C. Impact of large-dose vitamin A supplementation on childhood diarrhoea, respiratory disease and growth. Eur J Clin Nutr 1993;47:88–96.
14. Ramakrishnan U, Latham MC, Abel R. Vitamin A supplementation does not improve growth of preschool children: a randomized, double-blind field trial in south India. J Nutr 1995;125:202–11.
15. Allen LH. Nutritional influences on linear growth: a general review. Eur J Clin Nutr 1994;48:S75–89.
16. Smith JC Jr, McDaniel EG, Fan FF, Halsted JA. Zinc: a trace element essential in vitamin A metabolism. Science 1973;181: 954–5.
17. Smith JC Jr, Brown ED, McDaniel EG, Chan W. Alterations in vitamin A metabolism during zinc deficiency and food and growth restriction. J Nutr 1976;106:569–74.
18. Brown ED, Chan W, Smith JC Jr. Vitamin A metabolism during the repletion of zinc deficient rats. J Nutr 1976;106:563–8.
19. Mobarhan S, Greenberg B, Mehta R, Friedman H, Barch D. Zinc deficiency reduces hepatic cellular retinol-binding protein in rats. Int J Vitam Nutr Res 1992;62:148–54.
20. Smith JE, Brown ED, Smith JC Jr. The effect of zinc deficiency on the metabolism of retinol-binding protein in the rat. J Lab Clin Med 1974;84:692–7.
21. Morrison SA, Russell RM, Carney EA, Oaks EV. Zinc deficiency: a cause of abnormal dark adaptation in cirrhotics. Am J Clin Nutr 1978;31:276–81.
22. Russell RM, Morrison SA, Smith FR, Oaks EV, Carney EA. Vitamin-A reversal of abnormal dark adaptation in cirrhosis. Study of effects on the plasma retinol transport system. Ann Intern Med 1978;88:622–6.
23. Rahman MM, Mahalanabis D, Alvarez JO, et al. Acute respiratory infections prevent improvement of vitamin A status in young infants supplemented with vitamin A. J Nutr 1996;126:628–33.
24. Arifeen SE, Mahbub AQM, eds. A survey of slums in Dhaka metropolitan area: 1991. Dhaka, Bangladesh: International Centre for Diarrhoeal Disease Research, Bangladesh (in association with the Centre for Urban Studies, Dhaka University), 1993. [ICDDR,B working paper no. 39 (urban MCH-FP working paper no. 11).]
25. Rahman MM, Wahed MA, Fuchs GJ, Baqui AH, Alvarez JO. Synergistic effect of zinc and vitamin A on the biochemical indexes of vitamin A nutrition in children. Am J Clin Nutr 2002;75:92–8.
26. Bieri JG, Tolliver TJ, Catignani GL. Simultaneous determination of α-tocopherol and retinol in plasma or red cells by high pressure liquid chromatography. Am J Clin Nutr 1979;32:2143–9.
27. Mancini G, Carbonara AD, Heremans JF. Immunochemical quantitation of antigens by single radial immunodiffusion. Immunochemistry 1965;2:235–54.
28. Smith JC Jr, Butrimovitz GP, Purdy WC. Direct measurement of zinc in plasma by atomic absorption spectroscopy. Clin Chem 1979; 25:1487–91.
29. Jelliffe DB. The assessment of the nutritional status of the community. World Health Organ Monogr Ser 1966;33.
30. Rivera JA, Ruel MT, Santizo MC, Lonnerdal B, Brown KH. Zinc supplementation improves the growth of stunted rural Guatemalan infants. J Nutr 1998;128:556–62.