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Original Article

Effect of zinc supplementation on morbidity among stunted children in Indonesia

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Abstract

Background The Indonesian Health Ministry reported that 35.6% of Indonesian children and up to 50% in certain regions have stunted growth. They are at high risk of chronic zinc deficiency. Inadequate zinc intake may result in an impaired immune system and high incidence of morbidity. Zinc supplementation is known to improve immune status thus reducing the incidence of morbidity among stunted children.

Objective To evaluate the effects of zinc supplementation on morbidity incidence among stunted Indonesian school children.

Methods We evaluated the effects of daily zinc supplementation (2.38 mg of zinc-supplemented milk) on the incidence of diarrhea, respiratory infections, and fever in a double-blind, randomized, controlled trial in 169 stunted children (zinc-supplemented n=84; placebo n=85) aged 7 to 9 years in Jakarta and Solo. Zinc supplementation and morbidity surveillance were performed for 6 months.

Results Compared to the first 3 months of intervention, zinc supplementation resulted in a reduction in the incidence of diarrhea, respiratory infections, and fever during the second three months (by 67%, 42%, and 30%, respectively). Children from the zinc-supplemented group tended to have a lower episodic incidence of diarrhea and fever than those from the placebo group, although neither of these differences was statistically significant (P = 0.45, 95% CI 0.63 to 0.89).

Conclusion Zinc supplementation has no significant effect in reducing the incidence of diarrhea, respiratory infections, and fever in stunted children although tended to have a lower episodic incidence. **[Paediatr Indones. 2011;51:128-32-10]**.

Keywords: *Zinc supplementation, stunted, morbidity*

Inadequate nutrition in children may cause them to fail to achieve their genetically determined potential height, due to the poor quality of consumed food and high rates of infection. This condition leads to stunted growth or short stature.[1,2] It is likely that the nutritional inadequacies that cause stunting also impair host immunity, thereby increasing the incidence, severity, and duration of many infectious diseases.[2,3] Stunting is also used as an indicator of chronic malnutrition and its prevalence can be a historical depiction of nutritional status over a period of time. Stunting is a crucial indicator of success of development in a developing country.[2,4] The Indonesian Health Ministry reported that 35.6% children in Indonesia and approximately 50% in some regions were stunted.[4]

Zinc intake has been widely recognized as a significant factor in child growth and health in both developing and developed countries. Zinc deficiency, which is associated with impaired immune function, contributes to increased rates of morbidity among children.[5-8] Moreover, in children with severe zinc deficiency, the majority were stunted but this condition

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may be quickly reversed by zinc supplementation.[2,3] The International Zinc Nutrition Consultative Group (IZiNCG) has recommended strategies to control zinc deficiency and encourages more aggressive action in improving zinc status through supplementation, especially among those at high risk of inadequate intake or increased zinc requirements, such as during periods of rapid growth in childhood.[9] Eating rice as a main course may inhibit zinc absorption due to its high concentration of phytates. Furthermore, low consumption of high-zinc animal products puts Indonesian children at high risk for chronic zinc deficiency.[10,11]

Some studies of zinc supplementation in malnourished children have suggested improved growth and morbidity, but others have failed to identify any improvement in linear growth, despite impressive reductions in morbidity rates.[12] The aim of our study was to evaluate the effects of zinc supplementation on morbidity incidence among stunted Indonesian school children.

Methods

We conducted a community-based, randomized, double-blind trial in children aged 7 to 9 years from August 2007 to January 2008. Subjects were 188 poor children from elementary schools in Jakarta and Surakarta. Elementary schools were selected based on parental incomes and schools' fees as economic indicators. We included stunted children and excluded those with chronic illnesses, including renal disease, congenital heart disease, thyroid disease, chronic diarrhea and/or abnormal organ enlargement at the time of recruitment. Written, informed consent was obtained from all subjects and their parents. The Research Ethics Committee of Cipto Mangunkusomo Hospital and Moewardi Hospital approved this trial. Subjects were divided into two groups. The zinc-supplemented group received two, 54 g sachets of milk fortified with 2.38 mg zinc per day. The placebo group received milk containing 0.88 mg zinc.

All subjects underwent measurement of body weight and height, and filled out a record sheet on all food and drink consumed in the three consecutive days prior to the study. Weight was measured to nearest 0.1 kg with an electronic scale (SECA Corporation, Colombia, MD) and height to the nearest 0.1 cm with a Microtoire device. All measurements were taken twice and the mean value was used in the analysis. Z-scores for weight and height (weight-for-age, height-for-age, and weight-for-height) were calculated using EPI-Info version 3.4. Stunted growth was defined as height for age at 5-10th CDC percentile.[26] A 24-hour recall method was used in children, and the reported nutritional intake with this method was compared to the three-day food records survey for confirmation.[27] We used NutriSurvey for Windows (Copyright © 2003 Dr. J. Erhadt, Hohenheim University) to calculate intake energy and nutrient content per day.

All laboratory assessments were performed by trained observers at enrollment, and after 3 and 6 months. We obtained blood specimens by venipuncture at the beginning of the school session while subjects were in a non-fasting condition. Blood was collected in vacutainer tubes and processed within 2 hours. Plasma zinc was estimated by standard method using an atomic absorption spectrometer. Low plasma zinc level was considered to be < 10.7 μmol/L while serum zinc level of 12-18 μmol/L was considered to be normal.[13,14]

We evaluated the incidence of diarrhea, respiratory infection, and fever as indicators of morbidity in stunted children, due to its high mortality rate. Episodes of diarrhea was defined as subjects having three or more, loose or liquid *stools* per day. Respiratory infections were defined as the presence of at least two of the following symptoms: runny nose, cough, wheezing, difficulty breathing, or fever. Fever was defined as elevated temperature above 37.5 °C (100 °F). Incidence was defined as the number of new episodes within a specified period of time. Morbidity information was collected weekly, at the time of supplement distribution. A daily check list was used to record symptoms of illnesses observed during the previous 24 hours. The list included symptoms of respiratory infections (runny nose, cough, wheezing, difficulty breathing), gastrointestinal disorders (diarrhea based on mother's reports, number of stools/day, vomiting and presence of fecal mucus or blood), other infections, and selected complications of illness (apathy, anorexia, irritability, and fever).

Bivariate associations were analyzed using independent-samples t-test. $P<0.05$ was considered statistically significant. Statistical analyses were performed with SPSS-PC software (SPSS for Windows, version 15.0).

Results

From 188 subjects, 19 dropped out because of moving away or parental refusal. Ten of those 19 were from the zinc-supplemented group, while nine were from placebo group. There were 84 children in the zinc-supplemented group and 85 in the placebo group. Most of the children had low dietary zinc intake (< 60% RDA) (**Table 1**). However, mean plasma zinc levels in both groups were above the normal average in spite of subjects' severely low zinc intake. Plasma zinc levels decreased during the 6 months of the study to 10.42 μmol/L in the zinc-supplemented group and 10.18 μmol/L in the placebo group, but there was no significant difference between groups (P=0.12).

Table 1. Subjects' characteristics at baseline

	Zinc-supplemented (n = 84)	Placebo (n = 85)
Anthropometry		
Mean weight, kg	18.94	18.86
Mean height, cm	116.94	116.72
Laboratory results		
Mean hemoglobin, g/dl	13.08	12.83
Mean zinc level, μmol/L	13.48	13.29
Dietary intake <60% RDA, n (%)		
Calorie intake	55 (65.5)	55 (64.7)
Zinc intake	84 (100.0)	82 (96.5)
Iron intake	51 (60.7)	66 (77.6)
Calcium intake	66 (78.6)	77 (90.6)
Vitamin C intake	59 (70.2)	69 (81.2)

Children from the zinc-supplemented group tended to have a lower incidence of diarrhea and fever than those from the placebo group. The opposite was true of respiratory infections. However, none of these differences was statistically significant (P>0.05; **Table 2**). Compared to the first 3 months of intervention, we observed a reduction in the incidence of diarrhea, respiratory infections, and fever (by 67%, 42%, and 30%, respectively) during the second three months in the zinc-supplemented group.

Discussion

Most subjects in our study had low dietary zinc intake (< 60% RDA). They reported low consumption of high–zinc sources such as meat, seed-nuts, poultry, and eggs, possibly due to parental financial constraints. In spite of low zinc intake, they had plasma zinc levels above the normal average. Plasma zinc concentration is not considered to be a reliable indicator of mild or moderate zinc deficiency in individuals because homeostatic mechanisms maintain plasma zinc at a normal range except when zinc depletion is prolonged and severe.[15-18] Nevertheless, plasma zinc levels are still the most widely used biochemical indicator of a population's zinc status.[13,14,19]

We found a higher incidence of respiratory infections compared with diarrhea and fever in both groups. Both incidence and severity of respiratory infections have been reported to be increased in stunted children, and are an important determinant of mortality.[3,20,21] Stunted children tend to have reduced immunological capacity, especially in cellular

Table 2. Effect of zinc supplementation on diarrhea, respiratory infections, and fever

	Zinc-supplemented n = 84 (%)	Placebo n = 85 (%)	P value	Effect of Zinc 95% CI Lower	Upper
First 3 months of study					
Diarrhea	6 (0.07)	3 (0.04)	0.036	-.105	0.032
Respiratory Infections	52 (1.05)	45 (0.94)	0.616	-.446	0.233
Fever	23 (0.30)	18 (0.24)	0.162	-.213	0.088
Second 3 months of study					
Diarrhea	2 (0.02)	3 (0.04)	0.381	-.040	0.063
Respiratory Infections	30 (0.42)	26 (0.34)	0.170	-.254	0.103
Fever	16 (0.19)	18 (0.24)	0.140	-.089	0.178

immunity. Furthermore, this study was conducted in a low socioeconomic environment with poor environmental sanitation, perhaps contributing to the incidence of morbidity.

The beneficial effect of zinc supplementation on the incidence of morbidity has been reported in community-based studies in several countries, but studies in stunted children have been few.[1,5,12,20-23] We found no significant difference on the incidence of morbidity in both groups. There are several possible reasons for this observation. First, stunted children with chronic zinc deficiency may experience disruptions of the digestive tract, such as impaired intestinal brush border and perturbations in intestinal permeability resulting in interference of zinc absorption. Second, we used zinc doses below the recommended daily zinc intake for infants and young children (1 to 2 mg/kg/d). Although we counseled parents to improve their children's zinc intake and not depend on zinc supplementation, most subjects still consumed less than the recommended amount of zinc. Third, dietary components such as phytate and iron may interfere with zinc absorption. Supplementation of milk that we provided also contained iron at 6.56 mg in the zinc-supplemented group and 0.26 mg in the placebo group. It is possible that iron and zinc, when given together as a supplement, may interact with each other and compete for absorption in the small intestine.[24] Nonetheless, some studies showed that supplementation with iron and zinc combined was as effective as supplementation with iron alone and there were no adverse effects when iron and zinc were given together.[25]

In conclusion, zinc supplementation has no significant effect in reducing the incidence of diarrhea, respiratory infections, and fever in stunted children although tended to have a lower episodic incidence. Further study is needed to determine the benefits of zinc supplementation for reducing morbidity and mortality rates in stunted children.

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