Effect of Zinc Supplementation on Observed Activity in Low Socioeconomic Indian Preschool Children

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ABSTRACT. ***Objectives.*** **To investigate whether supplementation of zinc in preschool children is associated with improvement in observed activity levels.**

Methods. **On 2 consecutive days, we performed 5-hour observations with momentary time sampling (instant activity every 10 minutes) in children selected from an ongoing double-blind, randomized trial of zinc supplementation. The study was conducted in Kalkaji, a low-socioeconomic urban population of New Delhi with high diarrheal incidence and rates of malnutrition. A total of 93 children (48 zinc and 45 control) 12 to 23 months of age from an ongoing community-based, randomized, controlled trial received supplements for at least 1 month before study; 71% had received supplementation for more than 120 days. Zinc gluconate (10 mg of elemental zinc) was given daily, with both zinc and control groups receiving vitamins A, B1, B2, B6, D3, and E and niacinamide in addition.**

Results. **Outcomes were percentages of time spent in each of five activity levels and two groups representing high and low movement and overall rating by two activity scores. Children in the zinc group spent 72% more time performing activities in the high-movement group. Among the zinc-supplemented children, the activity rating by the children's activity rating score was 12% higher and by the energy expenditure score was 8.3% higher than in the control group.**

Conclusions. **In conclusion, zinc supplementation, given along with selected vitamins, was associated with significantly greater activity levels in children. The relationship between the activity increase and locomotor development needs to be investigated, as do the long-term implications of zinc supplementation in terms of developmental status and school performance.** ***Pediatrics*** **1996; 98:1132–1137;** ***zinc, activity, child development, malnutrition.***

ABBREVIATION. CARS, children's activity rating score.

Malnutrition in early childhood is associated with decreased activity and developmental delay.[1–4] Some of these effects in malnourished children may be the result of deficiencies of individual micronutrients. Zinc may be particularly important in this regard. Malnourished children commonly consume diets with low zinc content or with constituents that reduce bioavailability, or they have excess losses, eg, from diarrhea. Zinc deficiency in animal experiments has been shown to affect brain growth,[5,6] learning,[5–7] motivation,[6,8,9] memory,[10–12] and activity adversely.[5,13,14] Friel et al[15] found an improvement in motor development in low birth weight children given zinc supplementation. It is important to determine whether there are adverse effects in children in developing countries as a result of zinc deficiency. This information is of practical importance to determine the content of nutritional education, as well as to guide policy regarding fortification of foods or micronutrient supplementation for children in developing countries.

It has been hypothesized that reduced exploration in children contributes directly to diminished cognitive and motor development.[16–19] Despite uncertainty about a causal relationship between reduced activity and developmental lag, it is plausible that reduced activity may be an intermediate observable step in the process leading to developmental delays.

We investigated the effect of zinc on activity levels of children as a preliminary study to a full-scale assessment of development. We used a momentary time-sampling method modified from the methods of Gardner et al,[20] Torun,[21] and Puhl et al[22] to observe activity levels in a subsample of children selected from a double-blind, randomized, controlled trial of zinc supplementation.

METHODS

Population

The trial was conducted at Kalkaji, a low socioeconomic urban population of New Delhi. In this population, 94% of the women and 50% of men are illiterate. Among children 6 to 35 months old, 39% are stunted, and 7% are wasted (less than −2.0 z length for age and weight for length, respectively, compared with the National Center for Health Statistics reference population).[23]

Children and Randomization

Children 6 to 35 months old with diarrhea presenting to the dispensary at Kalkaji with reported passage of at least four unformed stools in the previous 24 hours, a diarrheal duration of less than 7 days, and permanent residence in Kalkaji were selected for inclusion. Exclusion criteria included children with malnutrition sufficiently severe to require hospitalization and those whose parents did not provide consent. Children could participate only once in the study.

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Before enrollment in the study, parents were given a full explanation of the study and signed informed consent. The study was approved by the human research review committees at All India Institute of Medical Sciences, the Johns Hopkins School of Hygiene and Public Health, and the World Health Organization.

Randomization schedules with permuted blocks of fixed length appropriate for double-blind studies[24] were used to compensate for seasonal variations in the disease prevalence and to prevent gross inequality of the number of allocations in stratified groups. Randomization was stratified by nutritional and breastfeeding status, as previously described.[23] Two separate randomization schedules were made by the World Health Organization for children to be followed only until the end of the diarrheal episode (short follow-up) and for children to be followed for 6 months after recovery from the enrollment episode (long follow-up). The two schedules were then combined to assure that allocation to short or long follow-up was also random. A sealed envelope contained the assigned group for each enrolled child.

Baseline Assessment

A detailed baseline assessment at enrollment included age, birth date, socioeconomic history, education of parents, and description of the feeding status. A physical examination, including hydration status, was performed by a physician. Weight was measured using SECA electronic scale with 10-g sensitivity (SECA Corp, Columbia, MD) by two independent observers; lengths were measured using Shorr length boards (Shorr Productions, Olney, MD) measuring to 0.1 cm. For dehydrated children, the weight was repeated after hydration.

Experimental Maneuver

Liquid preparations were made by Sandoz India Ltd (Bombay, India). Each 5 ml contained vitamins A (800 U), B1 (0.6 mg), B2 (0.5 mg), B6 (0.5mg), D3 (100 IU), and E (3 mg) and niacinamide (10 mg); in addition, the zinc preparation contained zinc gluconate (10 mg of elemental zinc). The bottles labeled with identification number and name were given to the mother and kept at the child's home. A separate team of field assistants dedicated to dispensing the assigned preparation visited the family every day except Sundays and holidays and fed the preparation to the child. They left a measured dose in a separate vial for the mother to feed on Sundays and holidays. A fixed dose of 5 ml per child was given daily for 6 months; during diarrheal illness this was increased to 10 ml to provide for excess zinc losses. If the child was going away from home, measured daily doses were provided for the duration of the trip. Of 90 421 days of follow-up, children were fed the supplement by a field worker on 78% of days in the zinc group and 79% in the control group. A family member fed the preparation on 19% of the days in the zinc group and on 18% of the days in the control group.

Follow-up Observation

The period of observation started on the date of recovery from the enrollment diarrheal episode and continued for 180 days. Each enrolled child was visited at home by a trained field worker every fifth day; if the child was not available on the scheduled day, the house was revisited the following day. Blood samples were collected for zinc estimation at enrollment and after 120 days of supplementation.

Activity Sample Selection

From the children enrolled in the main study, all children enrolled after September 1, 1993, 12 to 23 months of age and having received supplementation for at least 1 month were considered for selection. Children who had dropped out or had been away from home for more than 3 weeks during the month before selection were excluded. All 93 children fulfilling these criteria were selected. Of these, 71% had received supplementation for more than 120 days, 26% received supplements for 60 to 120 days and only 3% had received supplements for less than 2 months. At the time of the selection, the group allocations were double-blind.

Activity Assessment Procedures

Children were observed at home carrying out their usual activities. The momentary time-sampling assessment was done during an observation for a dietary intake study, and the mothers and children were not aware that activity was being recorded. Each child was observed for 5 hours between 9 AM and 2 PM on 2 consecutive weekdays. When a timer clicked every 10 minutes, the observer recorded the activity of the child at that instant. The activity record consisted of: (1) the place of observation (inside or outside the house); (2) the position of the child (carried, lying down, sitting down, standing, crawling, walking, running and jumping, or running jumping rapidly); and (3) the activity the child was performing at the observed time.

Observer Training

Two nutrition postgraduates were trained as observers. Training continued until both observers achieved 99% concordance (the percentage of the total number of observed events in which agreement occurred) with the trainer in five consecutive assessments. During pretesting and every 2 weeks during the study, concordance between the two observers was assessed by simultaneous 1-hour observation; it was always greater than 95%. Observers were unaware of group allocations. The observations were performed with crossover design such that for all children each observer assessed activity for 5 hours.

Data Recording and Analysis

The data from the activity assessments were coded daily by both observers together and were entered into a database. In addition to range and logical checks in the database, the printouts were checked manually by the supervisor who corrected entry errors. Double data entry was also performed.

A total of 93 children were observed (48 in the zinc group and 45 in the control group), with 4216 observations (2187 in the zinc group and 2029 in the control group). For each child the percent-

TABLE 1. Activities Performed by Children Classified According to the Effort

Stationary 1	Stationary 2	Slow Movement	Moderate Movement	Fast Movement
Scoring of activities according to CARS*				
1	2	3	4	5
Scoring of activities according to estimated energy costs as multiple of basal metabolic rate†				
1.2	1.2	2.0	2.5	3.0
Sleeping	Sitting down	Cleaning	Walking	Playing with active movements
Resting only	Babbling	Washing face	Crawling	Bathing and playing actively
Watching only	Watching and eating	Playing with little movement	Walking and eating	Eating and running in play
	Cleaning nose	Eating and playing with little movement	Dancing slowly	
	Sucking thumb	Bathing and playing with little movement	Playing with mud	
	Drawing	Crying with little movement	Walking and playing with little activity	

* Children's activity rating scale of Puhl et al.[22]

† The energy costs of grouped activities were estimated using data from Torun.[21]

age of time spent in each of the activities was calculated. The results were similar for the 2 days of observation, so for the final analysis observations for both days were pooled. The activities were grouped into five categories (Table 1). The highest level in the classification used by Torun,[21] "very heavy activity," was excluded, because children in the age range studied do not engage in these types of activities. The five activity levels were also combined into two groups representing the extent of movement: low movement (stationary 1, stationary 2, and slow movement) and high movement (moderate and fast movement).

Two activity scores were computed to compare the levels of activity using all data in a single analysis (Table 1). In both ratings the percentage of total time observed in each activity was multiplied by the factor representing energy expenditure; the products for all recorded activities were then summed. The children's activity rating score (CARS) has been previously validated.[22] The second score was based on the estimated energy cost of each category of activity. This method has been used previously[20,21] and is similar to the factorial method used to compute energy expenditure in adults.[25]

Statistical Methods

Statistical analysis was performed using Statistical Package for the Social Sciences PC+ (version 6.0) and Epi-Info (version 6.0) software. Anthropometric z values were calculated using Epi-Info (6.0), and the values were then appended to the data set. For each child the percentage of observed time spent in the five activity levels and the two movement groups (high versus low) was estimated. In addition, the two scores (representing an aggregate activity rating) were calculated for each child. Non–normally distributed data were log transformed.[26] Differences between zinc and control group children were then examined using Student's t test. For data that could not be normalized by log transformation, the Mann-Whitney U test was used to assess differences between groups. the χ^2 test and Fisher's exact test were used when appropriate to determine significance for baseline comparison. For multivariate analysis, logistic regression models were used. In these, group allocation (zinc or control) was modeled as the dependent variable, whereas the percentage of time the child was being carried or was performing a group of activities and potential confounders (age, breastfeeding, supplementation duration, stunting, sickness in the last 24 hours, fever on the day of observation, and proportion of days with diarrhea) were entered as independent variables.

RESULTS

Baseline Comparability Between the Groups

There were no significant differences between zinc and control group children for child, socioeconomic, and family characteristics as well as other baseline features that could have affected activity assessments (Table 2). The zinc group had slightly more stunted children (52.1% vs 44.5%).

Effect of Zinc Supplementation on Activity Levels

Zinc group children were observed to spend on average 72% more time in performing activities in the high-movement group than control group children (8.1% vs 4.7%; $P < .005$; Table 3). Among the zinc-supplemented children, the activity rating by the CARS was 12% higher ($P < .01$) and by the energy expenditure score was 8.3% higher ($P < .02$). These differences were significantly higher even after controlling for the time the child was carried, age, breastfeeding status, days receiving supplementation, baseline stunting (<-2.0 z/≥-2.0 z for height for age), sick in the last 24 hours (yes or no), fever on the day of observation (yes or no), and proportion of days with diarrhea. The zinc-supplemented children had 10.6 (SD, 5.4) observed eating events, compared with 12.7 (SD, 8.2) for control group children (not significant).

Effect of Zinc Supplementation on Activity by Gender and Stunting

The effect of zinc supplementation on activity was greater in male children. The percentage of time spent in the high-movement group in boys was 10.3 ± 6.3 in the zinc group, compared with 5.1 ± 4.5 in the control group (102% greater; $P < .01$). In boys the zinc group had an 18% higher CARS (153.2 ± 29.9 vs 129.3 ± 33.4; $P < .01$) and a 12% higher energy expenditure score (125.4 ± 16.3 vs 111.9 ±

TABLE 2. Baseline Comparison Between Children in Zinc and Control Groups Assessed for Activity

Feature	Zinc Group (n = 48)	Control Group (n = 45)
Total observation in group, n	2187	2029
Age on the day of observation, mo*	17.1 ± 4.5	17.1 ± 4.3
Missing visits in last mo ≤6 d†	44 (91.7)	43 (95.3)
Zinc level at enrollment, μg/dL*	61.7 ± 12.7	63.6 ± 20.3
Plasma zinc at enrollment, μg/dL†		
≤50.0	8 (16.7)	5 (11.1)
50.1–65.0	24 (50.0)	28 (62.2)
>65	16 (33.3)	12 (26.7)
Children in whom supplement was given for more than 24 of the 30 previous days†	47 (98.0)	44 (97.5)
Boys†	25 (52.1)	21 (46.7)
Breastfeeding at enrollment†	45 (93.8)	41 (91.1)
Nutritional status at enrollment†		
Normal	22 (45.8)	23 (51.1)
Stunted, not wasted	20 (41.7)	16 (35.6)
Wasted, not stunted	1 (2.1)	2 (4.4)
Wasted and stunted	5 (10.4)	4 (8.9)
Illness on day of observation†		
Cough	6 (15.4)	6 (14.6)
Diarrhea	9 (23.1)	9 (22.0)
Fever	4 (10.3)	3 (7.3)

* Mean ± SD.
† n (%)

TABLE 3. Comparison of Activity Indicators in Children Being Supplemented With Zinc or Control Preparations

Activity Indicator	Zinc Group (n = 48)	Control Group (n = 48)
Carried	17.7 ± 10.7*	16.9 ± 12.1
Stationary 1	48.7 ± 12.0	49.6 ± 14.5
Stationary 2	6.1 ± 4.0	7.0 ± 4.3
Slow movement	16.0 ± 7.3	15.1 ± 10.9
Moderate movement	5.4 ± 5.3	3.7 ± 3.8†
Fast movement	2.7 ± 4.0	1.0 ± 1.6‡
Movement group§		
Low	70.8 ± 9.0	71.7 ± 10.0
High	8.1 ± 6.4	4.7 ± 4.4‡
Rating using two scoring systems		
CARS method‖	144.2 ± 30.3	128.7 ± 33.5‡
Energy expense method¶	119.5 ± 16.1	110.3 ± 18.9†

* Mean ± SD.
† $P < .05$.
‡ $P < .01$.
§ Low group includes stationary 1, 2, and slow movement. High group includes moderate and fast movement.
‖ By children's activity rating scale, ie, proportion of time spent in each type of activity was multiplied by the weight assigned to that, and the values were summed to get the score for a child.[22]
¶ The energy costs of grouped activities were estimated using data from Torun.[21] The proportion of time spent in each type of activity was multiplied by the energy cost factor assigned to that group, and these values were summed to get the score for a child.

20.0; $P < .01$). The effect in the girls was not statistically significant. The effect of zinc supplementation tended to be greater in stunted children, but the differences were not significant (data not shown).

DISCUSSION

This study, the first of its kind, suggests that zinc deficiency may be an important determinant of the lower activity levels associated with malnutrition. These findings may have important implications for the cognitive and motor development of these children, but further studies are needed to draw definitive conclusions about the effect of zinc supplementation on child development. There may also be an implication of these findings for physical growth, because it has been shown in both rats and humans that increased activity leads to enhanced linear growth.[27]

There is now substantial evidence for a causal relationship between undernutrition and delayed child development.[1–4] Food supplementation in controlled trials leads to better development in children.[28] It is, however, not clear whether this benefit is due to a general dietary improvement or due to correction of a specific nutrient deficiency. The possible importance of zinc in child development was previously suggested by the improvements in developmental scores (especially in locomotor development) with zinc supplementation in low birth weight children.[15]

The specific mechanisms by which zinc affects activity or locomotor development are not yet clear. Zinc is one of the most prevalent trace elements in the brain.[29] It binds with proteins, maintains the functional integrity of synaptic events in the hippocampal mossy fibers,[15,30] and is important for both brain function and structural development.[30–32] Rats depleted experimentally by feeding dams a diet severely deficient in zinc during gestation and/or lactation have a variety of behavioral deficits, including decreased stress tolerance,[5,33] reduced activity,[34,35] impaired avoidance conditioning,[5,33] spatial learning deficit, and short-term memory impairment.[36] Morphological evidence of injury from zinc deficiency has been observed in the cerebella[30,37] of suckling rats.

The mechanism for the suggested greater effect of zinc supplementation in boys is also unknown. A similar sex difference in the effect of zinc supplementation on growth[38,39] and diarrheal morbidity[23] has been reported. A higher estimated zinc requirement in boys than in girls for infant growth has been suggested as a possible explanation for observed sex differences.[40]

The study of the relationship between physical activity and health among children has been hindered by a lack of agreement on objective measures of physical activity in field settings.[41] Methods for measuring activity in children include a self-report,[41,42] activity diaries,[43] use of motion sensors,[44] heart rate monitors,[45,46] and direct observation.[47,48] Direct observation methods have several advantages. They have been found to have high interobserver reliability and excellent correlation with assessment by motion sensors,[48] heart rates,[49] and calorimetry.[22] They are not limited by self-report and recall bias and do not require equipment that can hinder a young child's movement.[49] They, however, do have the problems of not being completely objective and requiring some form of time sampling.

Momentary time sampling has been shown to be superior to commonly used partial interval sampling by computer simulations and laboratory videotapes of actual behaviors[50–53] and to give a reasonably accurate estimate of the percentage time when brief intervals are used.[52,54] In this study, interobserver reliability was excellent, all children were observed by both observers, and observations were done at home in the children's usual environment. The presence of observers is unlikely to have greatly affected the children's behavior.

Scales and scoring systems should be validated, so we chose to use two systems that had had previous validation. Puhl et al[22] developed and evaluated a five-level CARS for use with young children. The CARS has been shown to have high interobserver reliability,[22,48] and correlation with caltrac motion sensor monitoring in children 2 to 6 years old.[48] Scoring based on energy cost developed by Torun[21] has been validated in two different settings.[20,21]

In conclusion, zinc supplementation, given along with selected vitamins, was associated with a significant increase in activity levels among children. This preliminary finding should stimulate further research to examine the implications of improved zinc status on activity, cognitive and locomotor development, and school performance. These findings, if confirmed, will have important implications for developing world settings where zinc deficiency in childhood is common. The effects of micronutrient deficiencies on development must be known to determine the educational messages to promote optimal infant feeding in developing countries. This knowledge will also help in the design of fortification of foods and nutritional supplementation programs.

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TEEN-AGE PREDATORS

Americans rightly believe that something fundamental has changed in our patterns of crime, namely the threat of serious crimes committed by youngsters who afterwards show us the blank, unremorseful stare of a feral, presocial being.

James Q. Wilson, Professor of Social Policy at UCLA, quoted in DeIulio, JJ Jr. Stop crime where it starts. *New York Times*. July 31, 1996.

Submitted by Student

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Effect of Zinc Supplementation on Observed Activity in Low Socioeconomic Indian Preschool Children

Sunil Sazawal, Margaret Bentley, Robert E. Black, Pratibha Dhingra, Sherly George and Maharaj K. Bhan

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