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The Effect of Zinc Supplementation on Linear Growth and Growth Factors in Primary Schoolchildren in the Suburbs Mashhad, Iran

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Abstract

Introduction

Zinc is an essential trace element required for the functional activity of several enzyme systems. Several studies have been carried out to assess the effect of zinc supplementation on children's growth, but controversy exists as to the effect of zinc on growth and growth hormone - insulin-like growth factor-I (GH-IGF-I) system. The aim of this study was to evaluate the effect of zinc supplementation on linear growth and serum level of IGF-I, Calcium(Ca), Phosphorus (P), Alkaline Phosphatase (ALP) in elementary school children living in a low socioeconomic suburbs of Mashhad, Iran.

Materials and Methods

The study was a randomized double-blind, placebo-controlled efficacy trial. Subjects were 200 volunteer primary school children. Both case and control groups comprised of 100 individuals each with 50 males and 50 females. Intervention supplementation was zinc sulfate tablets (10 mg elemental) and placebo tablets for both groups, administrated for a period of six months. The height, weight, height for age and weight for age Z-scores and Body Mass Index (BMI) were measured at 0, 2, 4, and 6 months. After six months the level of IGF-I, ca, p and ALP were measured using blood samples taken from 50 volunteer children, 33 from the case and 17 from the control group. The statistical analysis was performed by SPSS version 11.5.

Results

There was a significant increase in linear growth and weight amongst both male and female of the case group compared to the control after six months of receiving zinc($p<0.05$). However, there was no significant difference in the serum level for the measured parameters between the two groups.

Conclusion

This study provides evidence of positive effect of zinc supplementation on the growth of school children living in a low socioeconomic suburbs of Mashhad city in Iran.

Key Words: Alkalin phosphatase, Calcium, IGF-I, Linear Growth, Phosphorus, Zinc.

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Introduction

Zinc is an essential micronutrient for human growth. It is important for the metabolic activity of more than 200 enzymes including phosphatase, metaloproteinase, oxidoreductase and transferase, which are involved in protein synthesis, nucleic acid metabolism and immune functions. In addition, it is a structural component of various proteins, hormones and nucleotides. Zinc also plays an important role in transcription (1).

Zinc deficiency is reported to be associated with impairment of growth, testicular functions, appetite, taste, delay in wound healing, immune resistance, and memory. Zinc deficiency interferes with the metabolism of thyroid hormones, androgens and growth hormone (2, 3). Zinc also appears to be an important regulator of bone growth, bone repair, and ectopic bone formation through mechanisms that remain poorly understood (4).

However, it remains unclear how zinc deficiency relates to these changes at the biochemical level. Studies of zinc deficient animals have demonstrated that one of the mechanisms involved in the slowing down of growth is the low concentration of circulating IGF-I. It has been shown that serum IGF-I decreases with zinc depletion and increases again as soon as zinc is supplied in the diet, despite this, growth failure is not reversed by maintaining IGF-I levels through exogenous administration, suggesting that the defect must occur as a result of impairment of hormone signaling (1, 4).

A considerable number of intervention trials have been completed in different countries to assess the effect of supplemental zinc on children’s growth (5).

Serum zinc concentration may not always be a reliable indicator of an individual’s true zinc status. With small or moderate reduction in zinc intake, the serum zinc concentration is maintained within the normal range, and factors such as recent meal intake, infection and tissue catabolism can influence its concentration (5, 6).

Nevertheless, different studies have revealed inconsistent results. It appears that zinc supplementation has positive effects on growth in various groups of zinc deficient children (7-11), but in some studies the effect was not observed (2, 12-14), or if another supplementation like iron was added to zinc, the effect was apparent (15, 16). In some studies the effect of zinc on linear growth was shown only in either boys or girls (9, 17).

Other studies have also been carried out for evaluating the effect of zinc on GH-IGF1 system and bone formation markers, and their results are rather different (2, 7, 13, 18-20).

The aim of this study was to assess the effect of zinc supplementation on growth and bone formation markers in primary school children living in a low socioeconomic suburbs of Mashhad, Iran.

Materials and Methods

We designed a longitudinal double-blind, randomized clinical trial to detect differences in growth between supplemental(s) and placebo groups (p). We assessed the effect of zinc supplementation on linear growth, weight, serum levels of IGF-I, calcium, phosphorus and Alkaline Phosphatase in prepubertal school children.

The study was conducted in Altimor, a low socioeconomic suburb of Mashhad city in the Northeast of Iran. The performing organization was the department of Pediatrics in Emam Reza Hospital, a referral hospital in Mashhad city. This study was performed simultaneously with another study about the effect of zinc on common cold in

children with sample size of 200 (22) child aged 78 to 120 months, were randomly selected from an elementary school in Altimor, Suburb of Mashhad city.
The criteria for inclusion in the study comprised lack of evidence of both chronic disease and protein malnutrition. Children who received other mineral supplementation like zinc or iron were not included in the study.

They were randomly allocated to supplemental (50M, 50F) and placebo (50M, 50F) groups using systematic sampling. Fifty of the participants (33s, and 17p) volunteered to give blood after six months. The study was approved by the Ethics Committee of the Mashhad University of Medical sciences, and written informed consent to participate in the study was obtained from the parents of all children.

Procedure of trial

After baseline measurement of children's height and weight, intervention trial began in November 2004 to March 2005. Oral zinc supplementation (10 mg elemental zinc sulfate tablet) was administrated daily to the s group and placebo tablets to the p group, six days a week, for six month under the supervision of trained health workers of the school. Placebo and zinc tablets were identical in appearance and placed in containers labeled as A or B and given to the health workers for administration to children. Health workers, children and their parents were unaware that which tablet was zinc or placebo.

Regular field visits (once a week) for additional data collection and supervision of the health workers were made by the physicians. The height and weight were also measured at month 2, 4, and 6 following the administration. Fasting blood samples were obtained from 50 participants after six months. Serum IGF-I was measured by immunoradiometric assay. All samples were run in a single assay. Calcium, phosphorus and serum Alkalin phosphatase activity were measured by an auto analyzer. Data were analyzed using statistical software packages SPSS 11.5(SPSS, Inc, Chicago, IL) and Epi Info 2005(Center for Disease Control and Prevention, Atlanta, GA).

The mean weight, weight-for-age z score, height, height-for-age z score and BMI, measured at the start of study were compared with the same parameters measured 6 month later, by using paired t-test, in zinc and placebo group separately. Mean changes in the parameters during the 6 months trial, were compared between zinc and placebo group by using t-test. P-values of<0.05 were considered statistically significant.

Results

200 children of equal sexes participated in this study and were divided in two zinc and placebo groups. At entry to the study, the mean age of the male and female participants was respectively 91.78 ± 6.16 and 94.50 ± 8.21 months for the zinc group while this figure was 91.84 ± 5.9, and 95.64 ± 8.1 months for the placebo group.

The mean weight, weight-for-age Z score, height, height-for-age Z score and BMI, measured at the start and six months after receiving zinc or placebo are shown in (Table.1). All the measured parameters except height-for-age Z score in placebo group, increased during 6 months in both groups, and this increase was statistically significant ($p<0.001$). There was an increase in height in placebo group but the height-for-age Z score decreased during the trial.

The extent of changes of the parameters during the trial was compared between zinc and placebo groups. The increase observed in mean weight and height in the zinc supplemented children was significant compared to the control. Although BMI and weight-for-age Z score increased in zinc group more than the placebo one in both sexes, the increases were only significant in females. Increase in height-for-age Z score was significant in male participants who received zinc compared with those who received placebo supplementation (Table.2). The serum levels of IGF-I, calcium, phosphorus, and Alkaline phosphatase were measured in the blood samples taken from 50 children, six months after receiving Zinc. The serum levels of the parameters were compared between case and control groups and no significant difference was observed. The amounts of each parameter are shown in (Table.3).

Table 1: Mean weight, weight-for-age z score (WAZ), height, height-for-age z score (HAZ) and Body mass index (BMI) of the children measured at the beginning and 6 months following receiving zinc or placebo[1]

Type of Treatment		Baseline Level	Level after 6 months
Zinc			
Weight (kg)	F	21.13 ± 2.18	24.2 ± 2.59
	M	22.51 ± 3.18	25 ± 2.94
Height (cm)	F	121.19 ± 4.79	124.06 ± 4.8
	M	123.83 ± 5.59	126.67 ± 6.02
WAZ	F	-0.901 ± 0.71	-0.411 ± 0.65
	M	-1.113 ± 1.11	-0.657± 0.87
HAZ	F	-0.610 ± 0.803	-0.610 ± 0.785
	M	-0.731 ± 0.95	-0.723 ± 0.97
BMI	F	14.62 ± 1.79	15.54 ± 0.99
	M	14.28 ± 1.36	14.99 ± 1.34
Placebo			
Weight (kg)	F	21.05 ± 2.15	22.98 ± 2.28
	M	22.57 ± 3.01	24.64 ± 2.81
Height (cm)	F	121.41 ± 3.74	123.80 ± 3.78
	M	123.21 ± 5.14	125.2 ± 5.05
WAZ	F	-0.945 ± 0.65	-0.682 ± 0.6
	M	-1.21 ± 0.92	-0.89 ± 0.76
HAZ	F	-0.545 ± 0.61	-0.588 ± 0.68
	M	-1.02 ± 0.79	-1.13 ± 0.75
BMI	F	14.28 ± 1.36	14.99 ± 1.34
	M	14.85 ± 1.70	15.71 ± 1.48

F: Female, M: Male.

[1] Mean ± SD

Table 2: Rate of Growth and changes in height-for-age z score (HAZ), weight-for-age z score (WAZ), and Body mass index (BMI) of the children at 6 months of the study[1]

Variables	Female			Male		
	Zinc	Placebo	P-value	Zinc	placebo	P-value
Height (cm/6months)	2.87 ± 0.81	2.39 ± 1.117	0.02	2.84 ± 0.83	2 ± 0.96	<0.001
Weight (kg/6months)	3.07 ± 0.96	1.93 ± 0.76	<0.001	2.49 ± 0.95	2.07 ± 1.13	0.048
Δ HAZ	0.0002 ± 0.15	-0.042 ± 0.35	0.43	0.008 ± 0.15	-0.117 ± 0.18	<0.001
Δ WAZ	0.490 ± 0.33	0.262 ± 0.31	0.001	0.456 ± 0.42	0.316 ± 0.37	0.087
Δ BMI	1.32 ± 0.57	0.72 ± 0.57	<0.001	1.554 ± 0.99	1.571 ± 1.48	0.506

[1] Mean ± SD

Table 3: Serum IGF-I, Calcium, Phosphorus, Alkaline phosphatase of the children 6 month following receiving zinc or placebo[1]

Variables	Zinc	Placebo	P-value
IGF-I (ng/ml)	190.1±86.8	178.4±52.2	0. 61
Calcium (mg/dl)	10.35±0.57	10.63±0.77	0.15
Phosphorus (mg/dl)	5.06±0.62	5.04±0.41	0.92
Alkaline phosphatase (U/l)	292±60.9	299.6±75	0.7

[1] Mean ± SD

Discussion

Various studies have been carried out in order to investigate the effect of zinc supplementation on growth. The positive effect of zinc on growth has been shown in groups of zinc deficient children (7-11). Severe zinc deficiency can be determined by low concentration of zinc in plasma or hair, but there is no single sensitive test to determine mild zinc deficiency in humans, and the tests which are used currently do not always show the true zinc status of the body (5, 6, 14). Response to zinc supplementation in well randomized and controlled trials can be used as an effective indirect way to assess the level of zinc status in the body (5, 14).

Different studies have been carried out and their results are controversial (7-15, 17). In developing countries such as Iran, zinc deficiency is common due to plant-based diet which contains phytate as an zinc inhibitor and access to zinc rich food is also limited (11, 21).

So far, there is not much report on the zinc status of Iranian children and their need for supplementation, especially those of low socioeconomic status (11).

In our study, participants were 200 children who were living in a low income suburb of Mashhad, Iran. Although they were relatively healthy children, their mean height-for-age Z scores were -0.67 and -0.78 and their weight-for-age Z scores were -1.007 and -1.08 for case and control group respectively, according to National Center for Health Statistics (NCHS).

During six months of this double blind, placebo-controlled trial, there was an increase in height and weight parameters in the both zinc and placebo group, but the height and weight gain changes during the period were significantly higher in zinc compared to the placebo group.

This finding supports the positive effect of zinc which has been demonstrated to influence the growth of relatively healthy children (8, 10, 11) but differs from some studies in developing countries which have not shown any influence of zinc on growth, probably due to other growth limiting factors (14, 21-23).

In our study the effect of zinc supplementation on BMI and weigh for age Z score was significantly higher in females. On the other hand the effect on height for age Z score was significantly greater in males receiving zinc than placebo supplementation. This supports the finding of positive effect of zinc on growth velocity of boys with short stature (9), but differs from studies which the effect on height velocity was observed in females (17).

Although some studies have been carried out for evaluating the effect of zinc on GH-IGF-I system, the exact mechanism remains unclear (2, 7, 13, 18-20).

In some studies, zinc had positive effect on IGF-I or bone formation markers without changing the growth rate (2, 13). Other studies have shown positive effect of zinc on IGF-I, or other bone formation markers as well as an increase in the linear growth

(7, 18-20). However, some investigators have shown no change in the level of IGF-I but an increase in growth following zinc administration (1).

In this study, there was no significant difference in the amount of IGF-I, calcium, phosphorus and Alkaline phosphatase between case and control groups following administration of zinc or placebo for a period of six months. As we did not measure the baseline levels of the factors, their changes during six months couldn't be determined. In our study the side effects of zinc supplementation on children were mild gastroenteritis in three patients. This was resolved within few days.

Conclusions

Our study has shown that zinc supplement has positive effect on the gain of weight and height without adverse effect in the school children living in a low income suburb of Mashhad city in Northeast of Iran. We therefore recommend that zinc can be offered as an effective supplement with positive effect on children's growth especially in places of lower socioeconomic status.

The effect of zinc supplementation on BMI and weight-for-age Z score in females and height-for-age Z score in males requires further verification. However, a controlled trial study with a larger sample size is strongly recommended.

Conflict of interest: None.

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