Original Article

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Effects of Zinc Supplementation in Occurrence and Duration of Common Cold in School Aged Children during Cold Season: a Double-Blind Placebo-Controlled Trial

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Abstract

Objective: Zinc deficiency is common in children in developing countries due to low intake of animal foods, and high dietary phytate content. Zinc deficiency impairs overall immune function and resistance to infection. The effect of zinc on the common cold is still questionable. To determine whether supplementation of zinc could reduce frequency rate and duration of common cold during cold season in school aged children living in a low socioeconomic suburb of Mashhad (Altimor), north-east Iran.

Methods: We designed a randomized double-blind, placebo-controlled efficacy trial. Subjects were 200 grade 2 primary school children who all completed the trial. Intervention supplementation was zinc sulfate tablets (10 mg elemental) and placebo tablets for case and control groups, respectively. Tablets were taken on a daily basis, 6 days a week, for 5 months (November to March).

Findings: Among the zinc-supplemented group common cold incidence of 1.37±0.86 episodes per child during the study period was recorded in comparison to 3.15±0.55 cold episodes per child among the placebo group (P<0.001). Mean overall missing days from school was 0.55±1.09 days and 1.35±1.79 days for zinc-supplemented and placebo groups, respectively. The need for administration of antibiotics for bacterial infections (pharyngitis, acute otitis media, sinusitis, pneumonia) were 20 and 47 courses for zinc-supplemented and placebo groups, respectively (P<0.01).

Conclusion: This study showed that zinc supplementation has a beneficial impact on the occurrence of common cold.

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Key Words: Zinc Supplementation; Common cold; Upper respiratory Infection; Children

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Introduction

Zinc is an essential micronutrient for human growth, development, and immune function. Mild to moderate zinc deficiency can be best detected through a positive response to supplementation trials. Zinc supplementation has been shown to have a positive effect on the incidence of diarrhea, and pneumonia[1].

Upper respiratory tract viral infections are one of the most common reasons for physician visits. School aged children may experience 6 to 8 colds per year[2]. In children, this illness is also more extensive than in adults and usually requires medical attention. Statistics indicate that more than 80% of common colds requiring medical attention affect children and adolescents[3].

Zinc salts have been found to inhibit rhinovirus replication *in vitro*, possibly by interfering with rhinovirus protein cleavage[4]. It has also been suggested that cold symptoms, sneezing and nasal congestion, might be reduced by elevations in intranasal zinc salts, producing a chemical clamp, or may be due to correction of a subclinical zinc deficiency[5, 6].

Several controlled trials of treatment of common cold with zinc have been published; however, there are only a few community-based longitudinal studies that have been conducted with zinc supplementation for prevention of common cold during cold season[7].

To investigate the effect of zinc supplementation on the prevention of occurrence and the need for antibiotic administration, we performed an intervention trial among school aged Iranian children in suburb of Mashhad.

Subjects and Methods

The study was a randomized, double-blind, placebo-controlled, community-based intervention trial conducted between November 2004 and March 2005 in Altimor suburb of Mashhad, northeast Iran. The project was approved by the scientific advisory and ethical committees of Mashhad University of Medical Sciences. Written informed consent forms were signed by the parents before including the children in the study. For ethical reasons and limitation of cost we did not measure plasma Zink levels in this study.

A total of 200 children (aged 78 to 120 months) were randomly assigned to daily (6 days in week) supplementation with 10 mg elemental zinc as a tablet (n=100, 50 males, and 50 females), or placebo (n=100, 50 males, and 50 females).

For each child that was enrolled in the study, a standardized questionnaire was completed to obtain family details including basic demographic and socioepidemiologic data. The subjects were free of chronic diseases, such as sickle cell disease, or protein-energy malnutrition. All participants were observed on a daily basis for any medical sign and symptom especially cold symptoms. This daily surveillance for the detection of any sign and symptom of common cold and other possible diseases was conducted by trained health workers.

These workers were also responsible for proper administration of the zinc or placebo tablets. Regular field visits (once a week) for additional data collection and supervision of the health workers were made by our physician. Common cold was defined as the presence of at least two of the following symptoms: cough, headache, hoarseness, muscle ache, nasal drainage, nasal congestion, scratchy throat, sore throat, sneezing, and fever.

Data were analyzed using statistical software packages SPSS ll.5 (SPSS, Inc, Chicago, IL) and Epi Info (Center for Disease Control and Prevention, Atlanta, GA) using the χ^2 test ,*t*-test and ANOVA, *P* values less than 0.05 was considered statistically significant.

Findings

Table l summarizes the demographic characteristics of participants. The average occurrence of common cold was 1.73±0.86 in zinc recipients and 3.15±0.55 in placebo recipients ($P<0.001$)

Table 1: Demographic findings of 200 students treated with zinc sulfate or Placebo

Variable		Zinc group	Placebo group	*P* value
Age (month) Mean (SD*)		93.7 (7.38)	93.1 (7.35)	0.09
Sex	**Male**	50	50	
	Female	50	50	
Number of family members		4.7 (2.2)	4.5 (2.1)	0.7
Smoker Parent		18	19	0.1

* SD: Standard Deviation

(Table 2). Missing days from school during 5 months of study were 0.55±1.09 days (per student) and 1.35±1.79 days (per student) in zinc-supplemented and control groups, respectively (*P*<0.001). In the zinc-supplemented group, three participants complained from mild gastrointestinal discomfort which was resolved within few days and there was no need for their exclusion from the study.

Discussion

Millions of people throughout the world may have inadequate levels of zinc in their diet due to limited access to zinc-rich foods (animal products, oysters and shellfish) and the abundance of zinc inhibitors such as phytate, common in plant-based diets [8].

Zinc is a key component of the cell architecture and is required for the production of over 200 enzymes including phosphatase, metalloproteinases, oxidoreductase, and transferase which are involved in protein synthesis, nucleic acid metabolism, and immune function[18]. Zinc deficiency is common in young children in the developing countries and is associated with reduced immuno-competence and increased rates of serious infectious diseases[9]. Several studies have shown that zinc supplementation has a positive influence on linear, motor development and weight gain[19].

Community-based studies conducted among children of different age groups have shown the beneficial impact of zinc supplementation in the form of reduced diarrhea episodes in children with zinc deficiency, since this supplementation may lead to accelerated regeneration of mucosa, increased levels of brush border enzymes, enhanced cellular immunity, and higher levels of secretory antibodies [10].

Table 2: Median common cold occurrence need for antibiotic missing school Among 200 Students Treated with Zinc sulfate or Placebo

Variable		Zinc group	Placebo group	*P* value
Average common cold occurrence (SD)		1.7 (0.86)	3.1 (0.55)	<0.001
	Max	6	8	
	Min	0	0	
Need for antibiotic administration		20	47	<0.001
Days missing school		0.55±1.09	1.35±1.79	<0.001

* SD: Standard Deviation

We found that supplementation with zinc was associated with a decrease in the average occurrence of common cold during cold months of year, among children living in suburbs of Mashhad with low socioeconomic status. We also found that supplementation with zinc was associated with a decrease in the average duration and severity of common cold.

Prasad and coworkers showed a beneficial effect of zinc lozenges for reduction of duration and severity of cold symptoms[7]. They believed improvement in cold symptoms was related to the antioxidant anti–inflammatory effect of zinc[19].

However, previous trials failed to show a beneficial effect of zinc for treatment of common cold, perhaps because inadequate doses or inappropriate formulations of zinc were used, resulting in lack of bioavailable zinc[11,12]. Three other double-blind placebo-controlled trials evaluated the prophylactic and therapeutic efficacy of zinc gluconate glycine lozenges. In the first study involving 57 volunteers, administration of zinc gluconate lozenge (23 mg every 2 hours for 4.5 days) started one day before inoculation with human rhinovirus, reduced the total mean clinical score to 5.7 from 8.2 with placebo[13,14]. In another study 69 subjects were inoculated with human rhinovirus, and the 12 who experienced cold symptom were randomly allocated to receive either zinc gluconate lozenges or matched placebo every 2 hours for 6 days while awake. Once again zinc treatment significantly reduced clinical scores compared to placebo[15]. Retrospective chart analysis study by McElroy and coworkers provides strong support for the beneficial effects of zinc in school-aged subjects with common cold. They concluded that treatment with zinc can reduce duration of cold signs and symptoms and the need for antibiotics, and prophylaxis may decrease the incidence of colds[16]. Hulisz showed that zinc administration within 24 hours of the onset of common cold may reduce the duration and severity of symptoms of common cold[17]. According to American Family Physician guideline zinc is not recommended for treatment of common cold because of these inconsistent study results[20].

In our study only 20 participants in zinc supplementation group required antibiotics for treatment of upper respiratory tract infection compared to 47 individuals that needed antibiotic therapy in placebo group.

Recently, Kurugol and coworkers carried out a prospective study to determine the prophylactic and therapeutic effectiveness of zinc sulphate for the common cold in children. The results of the study showed that the use of zinc sulphate significantly reduced the risk of colds and cold-related school absences[3].

Conclusion

In conclusion we showed that supplemen-tation with zinc was associated with significant decrease of the frequency of colds, and reduction in the duration and severity of the symptoms of common cold. In addition, the need for use or misuse of antibiotics was reduced.

Fortification of more commonly used foods such as bread with zinc salts may be beneficial. However, further investigation is required.

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