Effect of zinc supplementation on preventing Diarrhea in children

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ABSTRACT

Introduction: Diarrhea still remains a leading cause of mortality in developing countries. Zinc has been reported to affect the treatment of acute gastroenteritis in children. This study was aimed at evaluating the prophylactic effect of zinc on prevention of diarrhea in children.

Methods: This randomized clinical trial was performed on 100 children of 6-36 months referring to Children Hospital outpatient clinic in Bandar Abbas who had no diarrhea during the study and no underlying medical condition such as celiac and allergy to cow's milk. The subjects were randomly divided into two 50-member groups of supplementation who received zinc sulfate for three months and control who received no drugs. All children were followed up every 3 weeks for one year. Gastroenteritis, type of diarrhea, and the duration of each episode were recorded. Data were analyzed with Chi-square and t-test.

Results: The mean age of the subjects was 21.5±7.9 months (ranged from 6 to 36 months); 61% of whom were male and 39% were female. There was no statistically significant difference between the two groups in terms of baseline characteristics and history of vaccination. The incidence of diarrhea, fever, and vomiting had no statistically significant difference between both groups (P=0.83, P=0.88, P=0.53, respectively). No significant difference existed between the groups in terms of the mean number of diarrheal episodes (P=0.96) and the duration of diarrhea (P=0.09).

Conclusion: The use of zinc for three months as prophylaxis had no impact on reducing the number and incidence of diarrhea in children aged between 6 and 36 months.

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Introduction:

Diarrhea is a treatable, preventable disease which still remains the leading cause of disease, disability, and death in the world especially in developing countries. Every year about 2 billion people suffer from diarrhea throughout the world, and this problem is more severe in children because during each episode of diarrhea essential nutrients are depleted from children's body which per se disposes them to malnutrition and failure to thrive (1). According to the World Health Organization statistics, nearly 21 thousand children less than 5 years expire due to preventable diseases (2) and 99% of these deaths occur in developing countries. Diarrhea is one of the main causes of death among the factors contributing to morbidity and mortality in children less than 5 years, and leads to an annual death of 0.801 million children under 5 years (3). It seems that the frequency of bacterial and parasitic

gastroenteritis has fallen which can be the result of improvement in public health infrastructure and nutritional status, use of plumbing for drinking water, and relative improvement of wastewater, however, viral gastroenteritis has not decreased and is responsible for about 3 to 5 percent of all hospitalization days and 7 to 10 percent of hospital admissions of children less than 18 years old (4). The World Health Organization and UNICEF have estimated an approximately 2.5 billion episodes of diarrhea each year in children less than 5 years in developing countries, with more than 80% of episodes in Africa and south Asia. Overall mortality may be declining, but the overall incidence of 3.6 episodes of diarrhea per child per year remains unchanged. Recurrent gastroenteritis of children can deplete nutrients essential for their growth, and as a result, diarrhea is one of the main causes of malnutrition (5).

The majority of children who are suffering from diarrhea are also malnourished, and malnutrition is associated with increased severity and duration of diarrhea. Children with diarrhea and malnutrition are often deficient in important micronutrients such as zinc; this can arise from inadequate intake of good quality and zinc-rich proteins or high intake of zinc absorption inhibitors such as phytate from plant food sources. In addition, zinc is highly excreted during intestinal diarrhea and hence exacerbates this micronutrient deficiency (6,7). Zinc affects the control of intestinal mucosa growth (8). The anti-diarrheal effect of zinc is related to stimulation of sodium absorption and inhibition of chloride secretion in epithelial cells, and affects three out of four ion secretion paths in the intestines and the control of acute diarrhea (9,10). With regard to these mechanisms and evidence on the effectiveness of zinc in reducing the duration and severity of diarrhea, the World Health Organization (WHO) and UNICEF has recommended the use of zinc in all rehydration solutions during episodes of acute diarrhea in children (11). In most studies, the effects of zinc have been investigated in the treatment of children with acute gastroenteritis, and it was effective in reducing the duration of diarrhea. However, studies carried out to prevent and control diarrhea have controversial results. In Bangladeshi children, using 10 days of supplementation reduced the frequency of diarrhea in the next three months, while it was ineffective in Nepalese children over six months (12,13). However, the effect of zinc in diarrhea prevention in children less than 5 years of age is unknown. This study aimed to evaluate the prophylactic effect of zinc on diarrhea in children referred to the Clinic of Bandar Abbas Children Hospital.

Methods:

This study is a randomized clinical trial and was conducted in the Children Hospital of Bandar Abbas. A total of 100 children aged 6 to 36 months were randomly selected from patients referred to the Hospital, providing that they had no diarrhea and underlying disease including celiac disease, inflammatory bowel disease, and food allergies for example to cow's milk at the time of enrollment in the study.

The researcher described the objective and implementation stages of the research project to parents of children who had the inclusion criteria, as well as details about the definition of diarrhea and vomiting, and mode and duration of the study; after their approval, they signed the informed consent form of Hormozgan University of Medical Sciences. The subjects were then randomly assigned into two 50-member groups based on the random numbers table; the supplementation group orally received zinc sulfate syrup (Alhavi pharmaceutical company; 10 and 20 mg for children less than and over one year, respectively) for prevention of diarrhea for 3 months, and the control group which received no supplement and was followed to the end of the study. Children were followed up by phone or in person by a pediatrician every three weeks for one year. Information about the outbreak of gastroenteritis, fever, and in cases of diarrhea, the number of defecation, and stool consistency were recorded. In case of severe vomiting and diarrhea, the patient was treated in the hospital emergency, and if the diarrhea was non-viral, antibiotic was prescribed by a pediatrician. Diarrhea was defined as three or more watery stools per 24 hours (14).

The obtained results were analyzed using SPSS-15. Quantitative variables were reported as mean±standard deviation and the qualitative variables as percentage. For all analyzes, $P<0.05$

was considered significant. Chi-Square and t-test were used for inter-group comparison of qualitative and quantitative variables, respectively.

Results:

The mean age of the subjects was 21.5±7.9 months (ranging from 6 to 36 months), and the subjects were composed of 61 boys and 39 girls. Complete vaccination was performed in 98% of the participants and there was no difference in vaccination between the two groups (P=0.67); one subject in each group had no complete vaccination. In terms of mean age, the supplementation group (21.6±8.2 months) had no statistically significant difference with the control group (21.4±7.6 months) (P=0.86).

By the end of the study, 41 patients (41%) developed diarrhea which was bloody in 1 child and watery in 40 children. No diarrhea was occurred during this period in 59% of the participants. Diarrhea was associated with fever in 6 patients (14.4%) and with vomiting in 23 cases (56.1%) in children who developed diarrhea.

As can be seen in Table 1, the two groups had no statistically significant difference in terms of the frequency of diarrhea (P=0.83), fever (P=0.88), and vomiting (P=0.53). During the follow-up period, one subject from the control group was hospitalized due to diarrhea but no hospitalization occurred in the supplementation group. The mean duration of diarrhea in children who received zinc and the control group was 5.8±1.2 and 4.6±2.3 days, respectively, and the difference was not statistically significant (P=0.09).

The mean number of defecation during the diarrhea period was 4.9±0/8 times per day in the zinc receiving group and 4.4±1.5 times per day in the other group, and no statistically significant difference existed between them (P=0.19). There was also no difference in the frequency of diarrhea between the two groups (P=0.97) (Table 2).

Table 1: Comparison of the Frequency of Diarrhea, Vomiting, and Fever during One Year of Follow-Up in the two Groups of Zinc Supplementation and Control

		Supplementation (%)	Control (%)	P-value
Diarrhea	Yes	30 (60)	29 (58)	0.83
	No	20 (40)	21 (42)	
Vomiting	Yes	13 (65)	10 (47.6)	0.53
	No	7 (35)	11 (52)	
Fever	Yes	3 (15)	3 (14.3)	0.88
	No	17 (85)	18 (85.7)	

Table 2. The frequency of diarrhea during one year of follow-up in the two groups of zinc supplementation and control

Diarrhea frequency	Supplementation (%)	Control (%)	P-value
Once	20 (74.1)	21 (72.4)	0.968
Twice	4 (14.8)	5 (17.2)	
Thrice	3 (11.1)	3 (10.3)	

Conclusion:

The results showed that the use of zinc supplementation in 6 to 36 months children was not effective in reducing the incidence of diarrhea as well in reducing the duration and frequency of diarrhea over one year compared with the control group, and no significant difference was observed in the frequency, rate, or duration of diarrhea.

The results of studies performed in children less than 5 years in different parts of the world are inconsistent so that the findings of Nepalese children are consistent with the findings of the present study (13), while Larson et al. showed that zinc supplementation can be effective in treatment and prevention of diarrhea in 9 months (15).

Most studies on the effects of zinc are about acute diarrhea and less addressed its prophylactic effect in a long time. Alam et al. followed 5-10 days zinc consumption in diarrhea in Bangladeshi children for three months, and found that zinc

supplementation for 5 days was as effective as 10 days (13). On the other hand, the nutritional status of children in the study was of the factors that have not been investigated and zinc may have beneficial effects only on malnourished children due to depletion of their zinc reserves, so that zinc was beneficial in the treatment of acute diarrhea in malnourished patients and zinc supplementation has reduced the number of defecation and duration of diarrhea (16). Children nutrition status and breastfeeding are factors affecting long-term studies of diarrhea and are effective in reducing the incidence of diarrhea in breastfed infants, which was not examined in this study and need to be investigated in future studies.

In our research, the mean duration of diarrhea in children who had diarrhea was 5.8±2.1 days in the zinc receiving group and 4.6±2.3 days in the control group. In a study by Hedayat et al. in Indonesia, this variable was 3.5±2.4 days in the consumer group and 3.8±2.6 days in the control group (17). Zinc supplementation had no significant impact on reducing the duration in none of the studies. Farooq et al. reported a significant difference between the zinc receiving group and the controls; and the mean duration of diarrhea was 6.1±5.1 and 7.1±5.1 days, respectively, and the difference was statistically significant. The mentioned studies were performed for treatment of acute diarrhea (18). Acute or chronic diarrhea, malnutrition, and breastfeeding can affect the results of studies. It seems that zinc plays a crucial role in acute diarrhea, while according to studies on chronic diarrhea, it has less important role in reduction of diarrhea duration. In a study in Peru, the duration of diarrhea was 2.2±1.7 days in the zinc group and 3±2.5 days in the control group, and this difference was statistically significant (19). In a research on chronic diarrhea in Pakistan, the duration of diarrhea was 5.1±3.3 days in the zinc receiving group and 5.5±2.7 days in the control group (20). In Bangladesh, it was 3.7±1.1 and 4.5±1.9 days in the zinc receiving group and the controls, respectively, and the difference was not significant (21).

The difference in the results of various studies can be attributed to the age groups studied, the study location, and the type of zinc salt used (22), and zinc may have beneficial effects on malnourished children (6, 23); measurement of zinc level at baseline would be very helpful. The limitations of this study include lack of investigating breastfeeding status, measurement of zinc concentration, and evaluation of zinc absorption in children. The issue of zinc deficiency in developing countries in which a large number of children are at risk of malnutrition is important. Most studies that have demonstrated the effect of zinc on diarrhea have been performed in developing countries in most of which children are suffering from malnutrition. Although Iran is also a developing country, differences in the nutritional status of the subjects may be the reason for insignificant results. In addition, due to the interaction of divalent salts such as iron and calcium as well as folate, fiber, and phytate on zinc absorption, more detailed studies are necessary to assess the bioavailability of this type of supplementation in children, and to teach the parents on supplementation of children in future studies.

In this study, the use of zinc had no significant impact on reducing the need for hospitalization and the number of diarrhea episodes during one year, and it seems that zinc supplementation for prophylaxis has no effect on the frequency, duration, and severity of diarrhea and the need for hospitalization.

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تاثیر مکمل یاری روی در پیشگیری از اسهال کودکان

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مجله پزشکی هرمزگان سال نوزدهم شماره اول فروردین و اردیبهشت ۹۴ صفحات ۱۷-۱۱

چکیده

مقدمه: *اسهال همچنان علت اصلی مرگ و میر در کشورهای در حال توسعه می‌باشد. اثر روی در درمان گاستروانتریت حاد کودکان گزارش شده است. هدف این مطالعه، بررسی تأثیر پروفیلاکسی روی در پیشگیری از اسهال کودکان بود.*

روش کار: *مطالعه کارآزمایی بالینی تصادفی در بین ۱۰۰ کودک ۶ تا ۳۶ ماه مراجعه‌کننده به درمانگاه سرپایی بیمارستان کودکان بندرعباس که در زمان مطالعه اسهال نداشتند و فاقد بیماریهای زمینه‌ای مثل حساسیت به شیرگاو و سلیاک بودند، انجام شد که به صورت تصادفی به دو گروه ۵۰ نفری تقسیم شدند. در گروه مکمل یاری سولفات روی به مدت سه ماه استفاده شد و گروه شاهد دارویی دریافت نکردند. کلیه کودکان هر سه هفته یک بار به مدت یک سال تحت پیگیری قرار گرفتند. وقوع گاستروانتریت، نوع اسهال، طول دوره ثبت شد. داده‌ها با استفاده از آزمون‌های آماری Chi-Square و t-test مورد تجزیه و تحلیل قرار گرفت.*

نتایج: *میانگین سن افراد مورد مطالعه ۷/۹±۲۱/۵ ماه بود (محدوده ۶ ماه تا ۳۶ ماه). ۶۱ نفر (۶۱٪) پسر و ۳۹ نفر (۳۹٪) دختر بودند. بین دو گروه مورد مطالعه از نظر خصوصیات پایه و سابقه واکسیناسیون اختلاف معنی‌دار آماری وجود نداشت. میزان بروز اسهال، تب و استفراغ در دو گروه از نظر آماری تفاوت معنی‌دار نداشت (به ترتیب P=۰/۸۳ P=۰/۸۸ P=۰/۵۳). میانگین تعداد دفعات وقوع اسهال (P=۰/۹۶)، طول دوره ابتلا به اسهال در دو گروه تفاوت قابل توجهی از نظر آماری نداشت (P=۰/۰۹).*

نتیجه‌گیری: *مصرف روی به مدت سه ماه به صورت پروفیلاکسی اثری بر کاهش تعداد دفعات و میزان ابتلا به اسهال در کودکان ۶ تا ۳۶ ماه نداشت.*

کلیدواژه‌ها: *روی - اسهال - کودکان*

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