Original Article

Clinical Effectiveness of Prophylactic Zinc on Growth, Pneumonia and Diarrhea in Children Less than 1 Year

Naima Batool, Salma Shaikh, Muhammad Nadeem Chohan

ABSTRACT

OBJECTIVE: To assess the impact of prophylactic Zinc supplementation in children on growth parameters (weight, length and, OFC) and the reduction of frequency of Diarrhea and Pneumonia.
METHODOLOGY: This Randomized Control Trial was done at EPI center in Outpatient department at Liaquat University Hospital, Hyderabad from April-November 2015. In this study, we randomly assigned 263 children aged 6 weeks to 1 year to receive either zinc or a placebo suspension orally during 5 months follow up visits. There were three refusals and 22 dropped out cases during the study. A total of 134 children received zinc and 129 received placebo. Data were analyzed and compared between two groups by calculating Mean and Standard Deviation of age, weight, length percentages of gender, frequency and percentages of diarrhea and pneumonia number of visits, episodes of fever.
RESULTS: The average percentage of ALRI was 8.9% in Zinc and 11.4% in Placebo group. Placebo group had high percentage of diarrhea for > 4 days than Zinc group in children. Placebo group had high percentage of Respiratory Infection for > 5 days than Zinc group in children. Placebo group had high percentage in Diarrheal episodes ≥ 3 in a month than Zinc group children. Both groups had same growth of length during Follow up visits. OFC development in both groups had not much difference. Both groups started earlier complimentary feeding with no big difference.
CONCLUSIONS: Prophylactic zinc supplementation had influence on growth parameters in children from six weeks to one year and showed decreased frequency of Diarrhea and Pneumonia.

KEY WORDS: Infants, Micronutrients, infections, Growth, Zinc

This article may be cited as: Batool N, Salma Shaikh S, Chohan MN. Clinical Effectiveness of Prophylactic Zinc on Growth, Pneumonia and Diarrhea in Children Less than 1 Year. J Liaquat Uni Med Health Sci. 2021;20(01):26-30. doi: 10.22442/jlumhs.2021.00646

INTRODUCTION

Zinc is a vital micronutrient in humans and is essential for protein function, cell development, and differentiation[1]. Regular dietary zinc intake is required because zinc cannot be produced or stored.[2,3] Tt is an essential mineral that is naturally present in some foods, added to others, and available as a dietary supplement. Zinc is also found in many cold lozenges and some over-the-counter drugs sold as cold remedies. Zinc deficiency is common in several developing countries; this is because the regularly staple diets are rich in phytates that are inhibitors of Zinc[8]. Our 30% world's population is deficient in Zinc, most prevalent in children under 5 years of age in developing countries[6].

Zinc deficiency is responsible for 4.4% of childhood deaths in Africa, Asia and Latin America[3]

Various studies showed that zinc-deficient populations are at increased risk of developing diarrheal diseases, respiratory tract infections, and growth retardation[1]. Diarrhea and pneumonia are the leading infectious causes of childhood morbidity and mortality. A high proportion of deaths occur in the first 2 years of life in both diseases, 23% for diarrhea and 15% for Pneumonia[4]. Meta-analyses studies showed that prophylactic zinc supplementation frequently diminishes the frequency of loose stools in children >12 months of age[5].

A daily intake of zinc is required to maintain growth because the body has no specialized zinc storage system. Prophylactic Zinc has been shown to be effective in decreasing both prevalence and incidence of Diarrhea, reducing respiratory infection and improving growth in children with impaired nutritional status[7]. Weekly zinc supplementation reduced the incidence of pneumonia and diarrhea in children, but there was a problem with its compliance[8].

Hypothesis of this this study was that Zinc supplementation as a prophylaxis reduces mortality and morbidity. The objective of this study was to assess the impact of prophylactic Zinc supplementation in children on growth parameters (weight, length and, OFC) and the reduction of frequency of Diarrhea and Pneumonia

METHODOLOGY

An analytical experimental study was conducted at EPI center in outpatient department at Liaquat University Hospital, Hyderabad from April to November 2015. Inclusion criteria was children aged between 6 weeks to 1 year of age of both genders.

The study was conducted among 263 children of Hyderabad city areas by Non probability purposive sampling. The study subjects included children aged 6

weeks to less than one-year age. All infants below the age of 6 months were on exclusive mother feed, while infants between 6 to 12 months took home made complementary food 3 times a day along with breast feeding. Ages of the children were confirmed mostly by using the child's birth certificate or immunization card. The purpose of the study was explained to the authority of those centers and all the respondents. To conduct the study, consent was taken from the mothers/guardians of the children.

Children were randomly divided into 2 groups. Random numbers were computer generated, by using variable length permuted blocks at the coordinating site using STATA 10 program. In the study the chief investigator and clients (parents) both were unaware about to whom zinc suspension was given and to whom placebo. It was all about in knowledge of staff nurse, who was arranged for this study. They were engaged to give one group zinc and other group placebo, and was keeping all the records confidentially.

In Group A Zinc supplementation was given for prophylaxis. In 6 weeks to < 6-month age of children, the dose of Zinc was (10 mg) 2.5 ml daily for 6 months and for six months to one year the dose was (20 mg) 5 ml daily for 6 months. [9] At every monthly visit length, Weight and FOC were monitored. History of fever, diarrhea and cough was also recorded at each monthly visit.

The data was collected in the study and analyzed it by using SPSS version 22. Categorical variables such as growth parameters, episodes of diarrhea and pneumonia their frequency, feeding practices, vaccinations, episodes of Fever were expressed in frequencies and percentages

All children from 6 weeks to 12 months of age whose mother, willingly agreed to come with every sickness of their child in our OPD were included in the study. Children treated already with Zinc, severely malnourished, immune deficient with celiac disease, cystic fibrosis or with any chronic illness were excluded from the study. The Sample size of this study is 263 children from 6 weeks to 12 months.

This study was conducted after approval from Ethical committee at Liaquat University Medical & Health Sciences, Jamshoro. Children who fulfilled the inclusion criteria were enrolled in the study. The purpose, procedure and benefits were explained and informed consent from the parents was taken. Two groups were made Group A and Group B and alternatively one patient was picked up from Group A and second from Group B and all the patients who were in Group A were given prophylactic supplementation of zinc according to age. The investigator of this study and parents of children they were kept un informed about dosages of zinc suspension and placebo in their respective groups the dose of zinc was 2.5ml (10mg) on daily basis, in < 6 months' children while it was 5ml (20mg) in > 6 months old children. Follow ups were visited every month up to 5 months and minimum numbers of visits were five. On each follow up the patient was asked and assessed according to Proforma. All the data was enrolled on preformed Proforma. If any child from group A or group B had got another dose of therapeutic zinc because of any diarrheal illness during whole intervention period, that child was dropped out from this study.

RESULTS

A total of 263 children were taken for the Study. As there were 3 refusals and 22 dropped out during study, all the children were enrolled. A total of 134 children received zinc and 129 received placebo (Table I). Mean length, weight and FOC was higher in Zinc group as compared to placebo group (Table II).

Number of follow-ups was 5 in each group and there was no occurrence of child death (Table I). Mostly < 3-month-old children were enrolled in both groups Zinc 89% and Placebo 95% than other age groups. 97.33% children in Zinc group were taking breastfeeding that is high than the placebo group. It was observed that both groups in 4th follow up has more default rate because our study was parallel with vaccination visits up to PENTA-II. After 3rd dose of PENTA, the next visit for MEASLES vaccine was at 9 months, that's why 4th follow up visit remained less in number. The average percentage of diarrhea in all visits in both groups was 11% in Zinc, 13% in placebo (Table III). The average percentage of Pneumonia was 11 (8.9%) in Zinc and 16 (11.4%) in Placebo group. Placebo group had high percentage of diarrhea for > 4 days than Zinc group in children. Placebo group had high percentage of Respiratory Infection for > 5 days than Zinc group in children. Placebo group had high percentage in Diarrheal episodes ≥ 3 in a month than Zinc group children (Table III). Both groups had same growth of length during Follow up visits (Table IV). OFC development in both groups had not much difference. Both groups started earlier complimentary feeding with no big difference. Infants < 6 months of both groups were on exclusive breast feeding and > months started complementary food along with mother feed.

TABLE I: DEMOGRAPHIC CHARACTERISTICS

Variable	Zinc Group	Placebo Group
Age (month) M(SD*)	1.81 (0.944)	1.6674 (0.75)
Gender n (%):		
Male	72 (54%)	77 (60%)
Female	62 (46%)	52 (40%)
Weight M(SD*) kg/gm	4.28 (0.74)	4.1481 (0.63)
Length M(SD*) cm	57.74(2.84)	57.22(2.87)
OFC M(SD*) cm	37.3(3.26)	37.5(1.502)

Characteristics		
Age	**Zinc Group**	**Placebo group**
<3months	89%	95%
>3 months	11%	5%
Feeding History		
Breastfeeding	97.60%	96.90%
Top Feeding	1%	2%
Follow Up		
1st Follow up	100%	100%
2nd Follow Up	99%	97%
3rd Follow up	98%	97%
4th Follow up	92%	91%

TABLE II: VARIATION OF WEIGHT, LENGTH AND FOC BETWEEN GROUPS

AGE	Group	Mean Weight (k/gm)	Standard Deviation	P-Value
<3months	Zinc	2.6363	0.738850	0.0001
	Placebo	1.9451	0.64515	
>3months	Zinc	2.7417	.56320	0.112
	Placebo	2.1714	.57071	
AGE	**Group**	**Mean Length (cm)**	**Standard Deviation**	**P-Value**
<3	Zinc	12.7204	2.75293	0.0001
	Placebo	10.9063	2.07277	
>3	Zinc	9.3333	2.75379	0.763
	Placebo	8.9583	2.10474	
AGE	**Group**	**Mean FOC (cm)**	**Standard Deviation**	**P-Value**
<3	Zinc	5.3474	.73685	0.0001
	Placebo	4.7187	1.19167	
>3	Zinc	4.9583	1.05439	0.333
	Placebo	4.6667	1.15470	

TABLE III: COMPLAINTS BETWEEN GROUPS

History of Diarrhea			P-Value
Visit	**Zinc Group**	**Placebo group**	
2nd Visit	12.69%	13%	0.583914
3rd Visit	10.45%	14%	
4th Visit	9.70%	10%	
5th Visit	11.19%	16%	
History of Pneumonia			
2nd visit	8.21%	12%	0.756718
3rd Visit	10.45%	16.28%	
4th Visit	11.19%	7.94%	
5th Visit	5.90%	9.02%	
Duration of Diarrhea			
No Diarrhea	84%	70%	0.003026
Diarrhea for One Day	1%	1%	
Diarrhea for two days	4%	4%	
Diarrhea for Three days	1%	3%	
≥ 4 days	9%	21%	
Duration of Pneumonia			
For 1 day	0.40%	0.60%	0.016623
For 2 days	1.70%	1.40%	
For 3 days	1.10%	1.70%	
For 4 days	2.10%	2.90%	
≥ 5 days	4.10%	12.60%	
Diarrhea episode in a month			
1 episode	9%	7%	0.020797
2 episodes	5%	10%	
≥ 3 episodes	2%	12%	
Pneumonia in a Month			
1 episode	6%	6%	0.878962
2 episodes	2%	5%	
≥ 3 episodes	1%	7%	
Started Complimentary Feeding at 6 months of age			
Yes	52.40%	48.06%	0.992511
No	47.76%	51.94%	
Continued Mother Feeding After Starting Complimentary Feeding			
Yes	76.87	76.74%	0.500184
No	23.13%	23.26%	

DISCUSSION

Benefits of Prophylactic zinc supplementation are well established on morbidity related to infections, however; there has been no attempt to quantify the effect of Prophylactic zinc supplementation on cause specific morbidity and mortality in children which is a new aspect in our review compared to previous reviews on the subject in preventive zinc supplementation[11].

In these 5 months follow up visits randomized control trial study, we have taken children for Zinc

TABLE IV: FOLLOW-UP PARAMETERS

	Weight Gain		P-Value
2nd Visit	98.50%	98.40%	0.007762
3rd Visit	97%	94.50%	
4th Visit	84.10%	78.90%	
5th Visit	80.30%	76.60%	
Growth in Length			
2nd Visit	99.30%	99.20%	0.278319
3rd Visit	99.30%	94.60%	
4th Visit	97.80%	97.70%	
5th Visit	97%	96.10%	
Growth in FOC			
2nd Visit	93%	89%	0.030466
3rd Visit	90%	87%	
4th Visit	80%	78%	
5th Visit	74%	73%	
History of Fever			
2nd Visit	7%	16.28%	0.004125
3rd Visit	10%	24.03%	
4th Visit	5%	13.95%	
5th Visit	5%	18.60%	

supplementation at 6 weeks to 1-year age and we divided in two age groups i.e. <3 months, and >3 months, the enrolment of children was high percentage in age group of <3 months in both groups Zinc 89% and Placebo 95%. There is no similar study has done yet. In this study 97.33% breast feeding children were registered than top feeding 1.5% in both groups

In the Present study the default rate was seen, also vaccination visits were missed during follow-up visits in some children in both groups.

During the Zinc Supplementation Diarrhea infection was seen in both group the average percentage was of Zinc group 11% in follow up visits and 13% in Placebo group.

In this study, Lower Respiratory Tract infection was found in both groups average percentage of Zinc was 8.9% and Placebo was 11.4 %, the similar study conducted by Christa L Fischer Walker and Robert E Black that Lower Respiratory Tract infection was indicated in both groups Zinc and Placebo[12]. Another study of cluster-randomized controlled trials showed diarrhea 18% and Respiratory Tract infections 19% during their study in both groups of children.

In this study the duration of loose stools in Diarrhea was also observed, that is more than 4 days in one group. It was also observed during study that Lower Respiratory Tract infection with number of days shown in both groups.[12] In this prophylactic zinc supplementation study, episodes of diarrhea and ALRI were observed in both groups [13].

Regarding weight between both groups, percentage and in table no: 2, it was shown the mean of weight gain. In zinc group it was 2.6363 and in placebo was 1.9451 and P-value was 0.0001 so the result was significant. As well as, it was also observed that Zinc group was high in linear growth than Placebo group. The mean of growth in length of Zinc was 12.7204 and Placebo was 10.9063 and P-value was 0.0001 so the result was significant[14-16].

This study also indicates that zinc supplement group was high than placebo group in OFC development in the children. The mean of OFC growth of Zinc group was 5.3474 and Placebo was 4.7187 and P-value was 0.0001 so the result was significant but there is no big difference.

In this study, Fever infection was also indicated in both groups during each follow up visits[17].

In this study the complementary feeding started after 5th month in both groups total average percentage was 52.5% and 47.5%. In this study the Mother feeding continued in both groups average percentage were 76.5% and 23.5% [18].

CONCLUSON

The present study showed a significant reduction in frequency of Diarrhea and ALRI in children age 6 weeks to 12 months after 5 months follow up visit with zinc prophylaxis. The outcomes of this study may influence to similar zinc-deficient populations too. Future trials on the effect of zinc prophylaxis on diarrhea and Pneumonia should focus on zinc-deficient children.

Ethical permission: Liaquat University of Medical & Health Sciences, ERC letter NO. LUMHS/REC/ =296, dated 30-3-2015.

Conflict of interest: There is no conflict of interest in authors.

Funding: There was no funding from any agency or institution.

AUTHOR CONTRIBUTIONS

Batool N: Concept, design, data collection
Shaikh S: Critical analysis, final approval
Chohan MN: Drafting, data analysis, critical review

REFERENCES

1. Aggarwal RI, Sentz J, Miller MA. Role of zinc administration in prevention of childhood diarrhea and respiratory illnesses: a meta-analysis. Pediatrics. 2007; 119(6): 1120-30.
2. Hotz C, Lowe NM, Araya M, Brown KH. Assessment of the trace element status of individuals and populations: the example of zinc

and copper. J Nutr. 2003; 133(5 Suppl 1): 1563S-8S.
3. Maggini S, Wenzlaff S, Hornig D. Essential role of vitamin C and zinc in child immunity and health. J Int Med Res. 2010; 38(2): 386-414.
4. Walker CLF, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, et al. Global burden of childhood pneumonia and diarrhoea. Lancet. 2013; 381 (9875): 1405-1416
5. Malik A, Taneja DK, Devasenapathy N, Rajeshwari K. Zinc supplementation for prevention of acute respiratory infections in infants: a randomized controlled trial. Indian Pediatr. 2014; 51(10): 780-4.
6. Liberato SC, Singh G2, Mulholland K. Zinc supplementation in young children: A review of the literature focusing on diarrhoea prevention and treatment. Clin Nutr. 2015; 34(2): 181-8.
7. Lamberti LM, Walker CLF, Chan KY. Oral Zinc Supplementation for the Treatment of Acute Diarrhea in Children: A Systematic Review and Meta-Analysis. Nutrients. 2013; 5(11): 4715–4740.
8. Maret W, Sandstead HH. Zinc requirements and the risks and benefits of zinc supplementation. J Trace Elem Med Biol. 2006; 20(1): 3-18.
9. Imdad A, Bhutta ZA. Effect of preventive zinc supplementation on linear growth in children under 5 years of age in developing countries: a meta-analysis of studies for input to the lives saved tool. BioMed Central Public Health. 2011; 11(3): S22.
10. Saper RB, Rash R. Zinc: An Essential Micronutrient. Am Fam Physician. 2009; 79(9): 768.
11. Tupe RP, Chiplonkar SA. Zinc supplementation improved cognitive performance and taste acuity in Indian adolescent girls. J Am Coll Nutr. 2009; 28(4): 388-96.
12. Sazawal S, Black RE, Bhan MK, Jalla S, Sinha A, Bhandari N. Efficacy of zinc supplementation in reducing the incidence and prevalence of acute diarrhea--a community-based, double-blind, controlled trial. Am J Clin Nutr. 1997; 66(2): 413-8.
13. Walker CLF, Black RE. Zinc for the treatment of diarrhoea: effect on diarrhoea morbidity, mortality and incidence of future episodes. Int J Epidemiol. 2010; 39(Suppl 1): I63–I69.
14. Shah UH, Abu-Shaheen AK, Malik MA, Alam S, Riaz M, Al-Tannir MA. The efficacy of zinc supplementation in young children with acute lower respiratory infections: a randomized double-blind controlled trial. Clin Nutr. 2013; 32(2): 193-9
15. Mayo-Wilson E, Imdad A, Junior J. Preventive zinc supplementation for children, and the effect of additional iron: a systematic review and meta-analysis. BMJ Open. 2014; 4(6): e004647.
16. Imdad A, Bhutta ZA. Effect of preventive zinc supplementation on linear growth in children under 5 years of age in developing countries: a meta-analysis of studies for input to the lives saved tool. BMC Public Health. 2011; 11: S22
17. Penny ME, Marin RM, Duran A, Peerson JM, Lanata CF, Lönnerdal B, et al. Randomized controlled trial of the effect of daily supplementation with zinc or multiple micronutrients on the morbidity, growth, and micronutrient status of young Peruvian children. Am J Clin Nutr. 2004; 79(3): 457-65.
18. Sandoval Jurado L, Jiménez Báez MV, Olivares Juarez S, de la Cruz Olvera T. Breastfeeding, complementary feeding and risk of childhood obesity. Aten Primaria. 2016; 48(9): 572-578.

AUTHOR AFFILIATION:

Dr. Naima Batool
Resident, Department of Pediatric
Liaquat University of Medical and Health Sciences
(LUMHS), Jamshoro, Sindh-Pakistan.

Dr. Salma Shaikh
Professor, Department of Pediatric
LUMHS, Jamshoro, Sindh-Pakistan.

Dr. Muhammad Nadeem Chohan *(Corresponding Author)*
Assistant Professor, Department of Pediatrics
LUMHS, Jamshoro, Sindh-Pakistan.
Email: nadeem.chohan@lumhs.edu.pk