ROLE OF ZINC SUPPLEMENTATION IN ACUTE DIARRHEA IN PRE-SCHOOL CHILDREN

Muhammad Younis Rao,Bashir Malik*, Ali Raza**

Pakistan Air Force Base Lahore Pakistan,*Combined Military Hospital Sialkot / National University of Medical Sciences (NUMS) Pakistan,**Pakistan AirForce (PAF) Hospital,Islamabad Pakistan

ABSTRACT

Objective: To monitor the therapeutic impact of zinc supplementation on clinical course of acute diarrhea i.e. frequency of stool, on stool amount and duration of acute diarrhea.

Study Design: Randomized controlled trial.

Place and Duration of Study: Family medicine department, PAF Hospital, Islamabad Pakistan from Jul to Dec 2009.

Material and Methods: One hundred and twenty eight children aged6 months to 60 months in an Outpatient pediatric department of PAF Hospital, E-9 Sector Islamabad with acute diarrhea of less than 14 days were included in this randomized controlled trial. They were further divided into two groups zinc supplemented group (n=65) and non-zinc supplemented group (n=65).

Results: Baseline characteristics were similar in both the groups. Mean age in zinc supplemented group was 33.67 ± 16.45 months and in non-zinc supplemented group 33.63 ± 16.44 months. Reduction in stool frequency per day was found 62% in zinc supplemented group and 26% reduction was found in non-zinc supplemented group with obvious difference of 36% between these two groups from day 3 to day 5, which was found statistically significant (p=0.01). Similarly, significant difference (p=0.01) was observed for reduction in amount of stool per day from day 3 and day 5 with obvious difference of 45% between the study groups.

Conclusions: Oral zinc administration in acute diarrhea reduces the frequency of diarrhea, output of stool and decreases total duration of diarrhea.

Keywords: Acute diarrhea, Amount of stool, Frequency of stool, Zinc supplements.

INTRODUCTION

Worldwide, diarrheal diseases are a leading cause of pediatric morbidity and mortality, with 1.5 billion episodes and 1.5–2.5 million deaths estimated to occur annually among children below 5 years of age[1] clinical trials show that zinc, as part of a treatment for childhood diarrhea, not only helps to reduce the severity and duration of diarrhea but also reduces the likelihood of a repeat episode in the future. Zinc is now included in the guidelines by the World Health Organization (WHO)/UNICEF for treatment of childhood diarrhea[2]. Scientist first hit on zinc's effectiveness in the early 1990s, when researcher from the Johns Hopkins School of Hygiene and Public Health in Baltimore gave children in New Delhi a daily dose of syrup containing 20 mg of zinc. The rate of diarrhea dropped dramatically[3]. That time WHO was concentrating on Malaria and HIV only for about a decade. Now the World Health Organization (WHO) has recommended that zinc must be used in the treatment of diarrhea. This study investigates the therapeutic impact of zinc supplementation on clinical course of acute diarrhea i.e. frequency of stool, on stool amount and duration of acute diarrhea.

MATERIAL AND METHODS

This trial randomized controlled was conducted at pediatrics department PAF Hospital Islamabad which is a 300 bedded hospital with a daily child outpatient attendance of about 200-250 over a period of 06 months. The children who were having three unformed stool within 24 hours and with the consent of parents, permanent

Correspondence: Muhammad Younis Rao, OC CMB PAF Base Lahore Pakistan (*Email: ok321dr@gmail.com)*
Received: 13 Dec 2013; revised received: 04 Jun 2015; accepted: 25 Jun 2015

residents of the study area and expected to remain in the area during the entire study period were included in the study. Children with illness requiring hospitalization, children who were likely to move away from study area during the study period and non-consent by the parents were excluded from the study. Probability random sampling technique was used to select 350 patients over a 06 month period. Three hundred and fifty pre-school children of both sexes aged 6 month to 60 months prepared to hospital with more than three unformed stools in 24 hours and diarrheal duration of <14 days.

Total 1050 patients had reported to pediatric department at PAF Hospital Islamabad during the study period. Out of these, 350 patients were selected for study. Out of these 170 children not fulfilling the inclusion criteria were excluded from the trial. So, 180 children were allocated for the trial. Among these, 90 were allocated in experimental group receiving zinc treatment(zinc syrup) and 90 were allocated in non-zinc group receiving no zinc treatment (zinc syrup). During hospital follow up, 25 patients were lost to follow up in experimental group and 25 in non-zinc group as they left hospital against medical

Table-I: Baseline characteristics of children of zinc supplemented and non-zinc supplemented groups.

Variables	Zinc supplemented group (n=65)		Non-Zinc supplemented group (n=65)	
Age in months				
6 - 12	18	28	16	25
13 - 36	21	32	19	29
37 – 60	26	41	30	47
Sex of child				
Male	33	51	30	46
Female	32	49	35	54
Socioeconomic status				
Upper	20	31	21	32
Middle	20	31	21	32
Lower	25	38	23	36
Diet of child				
Breastfed	33	51	32	49
Partially breast fed	30	46	27	42
Other milk	02	03	06	09
Mix feeding	00	00	00	00
Family diet	00	00	00	00
Diarrhea frequency/day on OPD				
≤ 5	11	17	09	14
6 - 10	46	71	45	69
> 10	08	12	11	17
No. of days for diarrhea on OPD				
≤ 7	59	92	60	94
8 – 14	06	08	05	06
Diarrhea with fever				
Yes	10	16	12	19
No	55	84	53	81
Diarrhea with vomiting				
Yes	09	14	12	19
No	56	86	53	81

advice. Finally, 65 patients remained for analysis in each of the groups.

All study participants patients were enrolled and divided in two equal zinc supplemented group and non-zinc supplemented group. All information was recorded on pre-designed and pre-tested questionnaire (appendix) attach appendix. Baseline data that was collected, included simple diarrhea with duration, frequency of stool, amount of stool, character of stool, age, gender, maternal education, family income, diet of child (mostly breastfed, partially breastfed, other milk, mixed feeding or family diet), immunization status, history of fever or vomiting, prior use of ORS, prior use of medications and nutritional status. All patients with dehydration were provided oral rehydration solution and zinc supplement as per WHO guidelines[4]. Height and weight were measured by a trained person. Infantometer was used to measure length of children below 24 months of age. Stool output was monitored by showing a small pill box (40 ml) as one unit[5].

Considering the objective of the study, all the collected data was tested against reduction in amount and frequency of stool per day, and was analyzed in both groupson day 3 and day 5 while comparing zinc supplemented group and non-zinc supplemented group. Baseline characteristics of both the treatment groups were entered, compared and analyzed by using Statistical Package for Social Sciences (SPSS Inc, Chicago, IL, USA) statistical software version 17[6]. Mean and standard deviations (SD) were calculated and statistical significance was tested by using Student's t-test.*p* value <0.05 will be considered significant.

Table-II: Impact of zinc supplementation on frequency of stool per day during follow up.

	Non- Zinc Group(n=65)		Zinc Group(n=65)	
Age group	**Day 3**	**Day 5**	**Day 3**	**Day 5**
6-12	5.89 ± 1.17*	3.33 ± 0.70*	5.22 ± 1.56*	2.11 ± 0.92*
13-36	4.63 ± 1.55*	2.59 ± 0.63*	4.65 ± 1.54*	2.03 ± 0.80*
37-60	3.78 ± 0.68*	2.39 ± 0.62*	3.78 ± 0.68*	1.46 ± 0.50*
Total	4.43 ± 1.36*	2.61 ± 0.70*	4.34 ± 1.33*	1.79 ± 0.75*

*= $p \leq 0.01$

p-value of baseline comparison is insignificant with $p=0.704$

Table-III: Impact of zinc supplementation on amount of stool per day during follow up.

	Non-Zinc Group(n=65)		Zinc Group(n=65)	
Age group	**Day 3**	**Day 5**	**Day 3**	**Day 5**
6-12	3.22 ± 0.70*	2.32 ± 0.52*	3.66 ± 0.70*	1.44 ± 0.52*
13-36	3.33 ± 0.76*	2.40 ± 0.50*	3.33 ± 0.67*	1.59 ± 0.50*
37-60	3.03 ± 0.50*	2.21 ± 0.40*	3.03 ± 0.50*	1.57 ± 0.50*
Total	3.25 ± 0.64*	2.34 ± 0.51*	3.25 ± 0.64*	1.56 ± 0.50*

*=$p \leq 0.01$

Baseline comparison is insignificant with *p*-value=1

Operational Definitions

Socioeconomic Status: Is a measure of an individual's or family's economic and social position based on education, income, and occupation. Categorized as upper, middle and lower class depending upon the level of education, income and occupation of the family[7].

RESULTS

Baseline characteristics of study group children are shown in table-I. Majority participants belonged to age 37 months to 60 months (41% in zinc supplemented groupand 47% in non-zinc supplemented group). Mean age in zinc supplemented group was 33.67 ± 16.45 months and in non zinc supplemented group 33.63 ± 16.44 months. There was an almost equal

socioeconomic distribution among study participants. In both the study groupsthe main finding was increased frequency of diarrhea (more than 10 times per day) with less than 7 days duration in pediatric department. Table-II shows the impact of zinc supplementation on frequency of stool in term of means comparison per day during follow up on day 3 and day 5 during acute diarrhea. Results showed that in all the age groups, stool frequency per day, which was the primary outcome variable, significantly reduced from day 3 to day 5 in zinc supplemented group as compared to the non-zinc supplemented group (table-II) from 2.61 ± 0.70 on day 5 to 1.79 ± 0.75. Reduction in stool amount per day (table-III) was found from 2.34 ± 0.51 on day 5 to 1.56 ± 0.50 with obvious difference between these two groups[8] (p<0.01).

Effect of zinc supplementation on stool amount per day is shown in table-III. All the stool evacuations were measured in numbers by showing a 40 ml stool container. Significant reduction in per day stool amount as primary outcome was observed from day 3 and day 5 while comparing zinc supplemented group and non-zinc supplemented group (p<0.01). Body weight and mid arm circumference measurement in the pediatric department and at day 5 was done but was statistically not significant. All patients were observed for any kind of adverse effects during trial by monitoring each patient carefully[9] (by examining the patient and by asking questions from the parents).

DISCUSSION

The findings of present study indicate that zinc supplementation in acute diarrhea effectively reduces both frequency of diarrhea and output of stool. It has been reported in the studyof zinc and copper supplementation in Bangladeshi childrenby Baqui[10], that those who received zinc supplementation during and after diarrhea had 24% shorter duration of diarrhea, 15% lower incidence of diarrhea.The diarrheal duration and frequency, primary concerns of the mother also do provide some valuable information regarding recovery. During the study it was found that the diarrheal frequency and duration was comparable in both groups initially, but on third day the zinc supplemented group had shown faster recovery in frequency and duration of diarrhea[11].

In another study by AB patel[12], it has been reported that most important predictor for duration of diarrhea in children was the severity of the disease at enrollment, and not the supplementation, but the present study showed no such role of disease severity. The reduction in duration of diarrhea episode is consistent with earlier studies[13].

In another study[14] it has been reported that combined zinc and vitamin A synergistically reduced the prevalence of persistent diarrhea and dysentery. Serum alkaline phosphatase measurementhas been suggested as an important surrogate marker of zinc status in human[15]. But we were not able to do the follow up study on the seventh and fourteenth day of supplementation.

This is the limitation of our study that rise in serum alkaline phosphatase with serial zinc supplementation was not followed as supported by other studies[16]. Both the groups were not given any other multivitamin or micronutrient supplement which may interfere with absorption of others and study results by their effect[17]. Present study was hospital based and only outpatient pediatric department patients were enrolled in the studyexcluding indoor patients. This was the limitation of present study leading to selection bias[18].

CONCLUSION

Oral zinc administration in acute diarrhea decreases the frequency of diarrhea and output of stool by changing the natural course of acute diarrheal disease, causes early normalization of stool consistency, early recovery and decreases total duration of hospital stay.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

REFERENCES

1. Patel A, Mamtani M, Dibley MJ, Badhoniya N, Kulkarni H. Therapeutic value of zinc supplementation in acute and persistent diarrhea: a systematic review. PLoS ONE 2010;5:e10386.
2. World Health Organization, WHO / UNICEF Joint Statement. Clinicalmanagement of acute diarrhea. Geneva: World Health Organization: 2004.
3. Brown KH, Peerson JM, Baker SK, Hess SY: Preventive zinc supplementation among infants, preschoolers, and older prepubertal children. Food Nutr Bull. 2009, 30 (1 Suppl): S12-40.
4. Lazzerini M, Ronfani L: Oral zinc for treating diarrhea in children. Cochrane Database Sys Rev. 2008, 005436
5. Aggarwal R, Sentz J, Miller, MA. Role of zinc administration in prevention of childhood diarrhea and respiratory illness: a metaanalysis. Pediatr: 2007; 119: 1120-30.
6. Boschi-Pinto C, Velebit L, Shibuya KI.Estimating child mortality due todiarrhea in developing countries. Bull WHO: 2008; 86:710–17.
7. Trivedia SS, Chudasamab RK, Patel N. Effect of zinc supplementation in children with acute diarrhea: Randomized double blind controlled trial. Gastroenterol Res 2009;2:168-74.
8. Alves CX, Vale SH, Dantas MM, Maia AA, Franca MC, Marchini JS, Leite LD, Brandao-Neto J: Positive effects of zinc supplementation on growth, GH, IGF1, and IGFBP3 in eutrophic children. J Pediatr Endocrinol Metab. 2012, 25 (9–10): 881-887.
9. Oteiza PI: Zinc and the modulation of redox homeostasis. Free Radic Biol Med. 2012, 53 (9): 1748-1759.
10. LopezAD, Mathers CD, Ezzati M, JamisonDT, Murray CJ. Global andregional burden of disease and risk factors: systematic analysis of population healthdata. Lancet:2006; 367:1747–57 (PMID).
11. AKU, PMRC, Nutrition wing Ministry of Health Pakistan. NNS: National Nutrition Survey ofPakistan. Supported by UNICEF Pakistan. 2011
12. Lazzerini M, Ronfani L. Oral zinc for treating diarrhea in children. Cochrane Database Syst Rev 2008:CD005436.
13. Rehman MM, Mohammad AW, George JF, Abdullah HB, Jose OA. Simultaneous zinc and vitamin A supplementation in Bangladeshi children: randomised double blind controlled trial. BMJ: 2001; 323: 314.
14. Iwaya H, Kashiwaya M, Shinoki A, Lee JS, Hayashi K, Hara H, et al, Marginal zinc deficiency exacerbates experimental colitis induced by dextran sulfate sodium in rats. J Nutr. 2011, 141 (6): 1077-82.
15. Podewils LJ, Mintz ED, Nataro JP, Parashar UD. InfectiousDiseases of children in developing countries:acute, infectious diarrhea among children indeveloping countries. Semin Pediatr Infect Dis: 2004; 15:155–68.
16. Robert BS. Zinc: An EssentialMicronutrient.Am Fam Physician:2009; 79(9):768-72.
17. Brown KH, Baker SK . Galvanizing action: conclusions and next steps for mainstreaming zinc interventions in public health programs. Food Nutr Bull 2009; 30: S179–84.
18. Scrimgeour AG, Lukaski HC. Zinc and diarrheal disease: Current status and future perspectives. Curr Opin Clin Nutr Metab Care 2008;11:711-7.