Original Article

Effect of Zinc Supplement on Severity of Acute Diarrhea Among Children Under Five Years of Age

Shaista jabeen[1*], Tanzeel Shafique[1], Shahnai Basharat[1], Anees Ahmed Khalil[1], Muhammad Ali[2], Mudasir Saeed[3] and Numan choohan[4]

[1]University Institute of Diet and Nutritional Sciences, Faculty of Allied Health Sciences, The University of Lahore, Lahore, Pakistan
[2]Newfold University, Canada
[3]International Education College Chinese and Western Medicine Clinic, Dalian Medical University China, Dalian, Liaoning, China
[4]Department of Biochemistry, University of Agriculture, Faisalabad, Pakistan

ARTICLE INFO

ABSTRACT

According to World Health Organization (WHO) approximately four million children less than 5 years of age in Asia, Africa, and Latin America die annually from diarrhea; and 80% of these deaths occur in the first year of life. **Objective**: To evaluate the effect of zinc supplement on the severity of acute diarrhea in children under the age of five years **Methods:** Children with diarrhea were included. Zinc was randomly assigned to diarrheal patients in different concentrations: 5 mg, 10 mg, 15 mg and 20 mg. There were two groups in our study, treatment and control group. The results are presented in the form of descriptive and inferential statistics. **Results:** In T1 (Treatment Group) number of Diarrhea patients < 1 Year of age were 16, 2–4 years of age were 45, 4–5 years of age and maximum no of patients in T1 < 2 year of age were 57. Numbers of male patients were 84 while female patients were 67 in T1. In T2 (Control Group) number of male patients were 92 while female patients were 59. In T1 number of patients residing in urban area were 51 while rural were 100. In T2 number of urban were 69 while rural were 82. Number of patients stay in the hospital for one day was 67, 15 for Four days and only 1 for seven days in T1. In T2 number of patients stay in the hospital for one day were 29, 17 for four days and only 6 for seven days. In T1 number of Patients with watery diarrhea was 87, Mucoid consistency of stool was 31, soft consistency of stool was 23 and formed consistency of stool was 9. In T2 watery diarrhea was 92, Mucoid consistency of stool was 25, soft consistency of stool was 31 and formed consistency of stool was 4. Frequency of stool significantly reduced (P<0.005) at 7th day of zinc treatment while consistency of stool was significantly improved (P<0.005) at day 3 and day 5 of zinc treatment. **Conclusions:** Children who received zinc supplements showed a marked improvement in all outcome measures, suggesting that this deficiency is amenable to correction by replacement.

INTRODUCTION

Diarrhea is defined as the passage of three or more loose stool in 24 hour period; diarrhea may be acute lasting less than two weeks or persistent lasting for two weeks or longer or chronic lasting more than four weeks [1]. Diarrhea is cause for 18% of deaths in children age group and the most common cause of acute diarrhea in all children is Rota-virus. Diarrhea that persists for more than two weeks is chronic diarrhea; it is caused by intestinal infection mainly in developing countries [2]. 1.7–5 billion cases of diarrhea occur per year [3], but total deaths from diarrhea reported in 1990 were 2.58 million; declined to 1.26 million in 2013 [4]. The prevalence of childhood diarrhea in Pakistan is reported as 51%. Varieties of micro organisms, including bacteria, parasites & viruses out of which viruses have been extensively studied in recent years. The commonest causative organism is Rota virus and is responsible for 29% of all diarrheal deaths in children less than 5 years of age, in Indian Sub-Continent 1/4th of children suffer from same [5]. Percentages of children experiencing co morbidity (defined in this study as presence of both diarrhea and ARI) were highest in developing countries including Pakistan [6].

In developed countries, diarrheal diseases also constitute an important cause of morbidity and mortality. According to World Health Organization (WHO) (Data from 2008) approximately four million children less than 5 years of age in Asia, Africa, and Latin America die annually from diarrhea and 80% of these deaths occur in the first year of life [7]. In humans, zinc is a vital micro nutrient essential for protein synthesis, cell growth, and differentiation known as apro-antioxidant and anti-inflammatory agent [8]. Treatment of

acute diarrhea with oral rehydration solution has become widespread, resulting in reduced mortality from dehydrating diarrheas but no decrease in the duration of episodes or their consequences, such as malnutrition [9]. Furthermore, adherence to recommendations regarding fluid therapy in children with diarrhea is poor because care givers want to reduce the duration of illness and this often leads them to use antibiotics and other treatments of no proven value [10]. World Health Organization (WHO) and the United Nations Children's Emergency Fund (UNICEF) jointly released a statement in 2004 to emphasize the use of oral zinc to reduce the incidence of diarrhea and its severity in children less than five years of age [11]. Contaminated and unhygienic weaning foods may lead to diarrhea in children [12,13]. Infants may also be exposed to these pathogenic organisms including rota virus, in case of un-hygienic weaning diet [14,15]. Sanitation is a major factor for severity of diarrhea in developing countries [16-21]. Zinc is present in a wide variety of foods, but in most developing countries children have a low intake of foods rich in readily absorbable zinc, such as liver, red meat, poultry, fish, cheese, nuts, oysters and crat's [22].

Cow's milk because of its high level of case in and calcium, and soya milk, because of its phytate content, may further reduce the absorption of zinc from diet, in contrast, zinc in breast milk is well absorbed. Vegetable and fruits contribute very little to dietary zinc intake, but fruits eaten with cereals may increase the bio availability of zinc. Zinc iron, and other minerals compete with one another for absorption because they share the same absorption path ways [23]. A recent study from China showed that 46.48% of diarrheas among young children are due to viral etiology with Rota virus infections were the most common, followed by adeno virus infections, noro virus infections and astro virus infections. Children younger than one year old were the most susceptible population to viral infections (87.9%) [24].

M E T H O D S :

This study was randomized controlled trial conducted in Department of Pediatrics, Mansora Hospital. The duration of study was 12 months. Children who were suffering from acute diarrhea, aging 1-5 years were selected. Children who suffered from any other health complication rather than acute diarrhea were excluded from the study. There were 302 participants who meet the study criteria were randomly assigned into two groups. The intervention group (n=151) and control group (n=151). The intervention group was assigned mg/day for days and the control group was not given zinc supplement.

At baseline visit, a questionnaire was filled to verify the inclusion criteria. The questionnaire comprised of patient's complaint at the time of admission which includes vomiting, diarrhea duration, consistency and frequency were taken.

The past history and nutritional history were taken. The post study questionnaire data was collected from both groups after 15 weeks.

In the intervention groups 106 participants who completed the study. Two participants in treatment group and four participants in control group left the study due undefined reasons. In control group 104 participants who completed the study and were analyzed.

Data Analysis

Data was analyzed and entered in the SPSS version 21. The results were presented in the form of descriptive and inferential statistics. Frequencies and the percentages were reported for categorical variables while the mean and standard deviation was reported for continuous variables. Validity of the tool was checked by content validity. T-test was used to compare the base line and treatment data. The proportional differences of categorical variables were compared by applying chi-square test. P value 0.05 was considered as significant.

RESULTS:

Figure 1 shows, in T1 (Treatment Group) number of Diarrhea patients < 1 Year of age were 16, 2-4 years of age were 45, 4-5 years of age and maximum no of patients in T1 < 2 year of age were 57. In T2 (Control Group) minimum number of Diarrhea patients < 1 Year of age were 14 while < 2 year of age were 52, 2-4 years of age were 49 and 4-5 years of age were 36. Treatment Group (T1) had 84 male patients and female patients were 67. In Control Group, T2, number of male patients were 92 while female patients were 59.
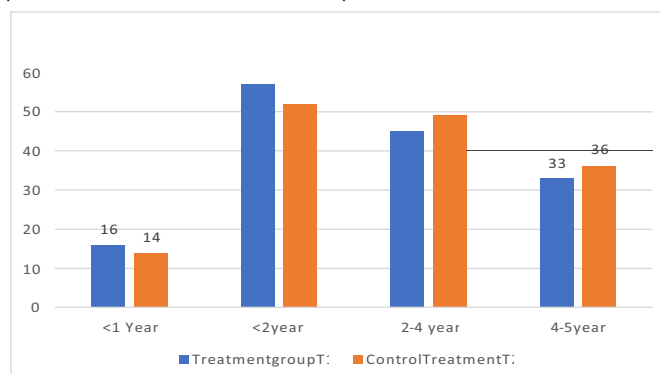

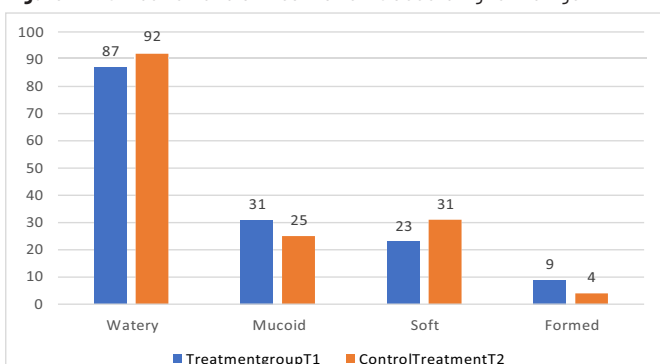**Figure 1:** Distribution of diarrheal Patients according to the Age

Figure2: Distribution of Diarrhea Patients according to the Consistency

Figure 2 describes that in T1, number of Patients with watery diarrhea were 87, Mucoid consistency of stool were 31, soft consistency of stool was 23 and Formed consistency of stool were 9. In T2, watery diarrhea were 92, Mucoid consistency of stool were 25, soft consistency of stool were 31 and Formed consistency of stool were 4.

Frequency		
Duration	**T1Group**	**T2Group**
3 Days	36	50
7Days	88	79
10 Days	27	22
Total	151	151

Table 1: Distribution of Diarrhea Patients according to the Duration of Diarrhea

Groups	On Admission			After Treatment		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Treatment GroupT1	2	4	145	124	2	25
Control groupT2	20	21	110	126	4	21

Table 2: Distribution of Diarrhea Patients according to the Assessment of Dehydration on Admission

In T1, number of patients with severe dehydration were 147, moderated dehydration were 4 and with mild dehydration were 2. In T2, patients with severe dehydration were110, moderate dehydration were 21 and with mild dehydration were 2. After treatment dehydration level in T1 (Treatment Group) number of Patient with mild dehydration after treatment were 124, with moderate dehydration were 2 and with severe dehydration were 25. In T2 (Control Group) number of Patient with mild dehydration after treatment were 126, with moderate dehydration were 4 and with severe dehydration were 21 (Table 2).

		Amount of zinc given						
	Frequency of stool	5mg	10mg	15 mg	20 mg	**TotalT1**	**TotalT2**	**P- value**
Day 3	1–3	0	1	0	0	1	0	0.164
	4–7	2	33	33	14	82	66	
	8–10	7	23	28	6	64	78	
	>10	1	3	0	0	4	7	
	Total	10	60	61	20	151	151	
		Amount of zinc given						
	Frequency of stool	5mg	10mg	15 mg	20 mg	TotalT1	TotalT2	P- value
Day 5	1–3	2	14	42	13	71	21	0.177
	4–7	6	38	18	06	68	111	
	8–10	2	7	1	0	10	17	
	>10	0	1	1	0	1	2	
	Total	10	60	62	19	151	151	
		Amount of zinc given						
	Frequency of stool	5mg	10mg	15 mg	20 mg	TotalT1	TotalT2	P- value
Day 7	1–3	2	37	51	18	108	72	0.000
	4–7	8	22	10	02	42	77	
	8–10	0	1	0	0	1	1	
	>10	0	0	0	0	0	1	
	Total	10	60	61	20	151	151	

Table 3: Distribution of diarrhea 1 Patients according to the Frequency of stool.

		Amount of zinc given						
	Consistency of stool	5mg	10mg	15 mg	20 mg	TotalT1	TotalT2	P- value
Day 3	Watery	5	15	3	1	24	43	0.001
	Soft	2	37	17	12	68	75	
	Formed	1	2	0	2	5	4	
	Semisolid	2	5	41	5	53	24	
	Mucoid	0	1	0	0	1	5	
	Total	10	60	61	20	151	151	
		Amount of zinc given						
	Consistency of stool	5mg	10mg	15 mg	20 mg	TotalT1	TotalT2	P- value
Day 5	Watery	1	1	0	0	2	7	0.000
	Soft	8	17	1	1	27	61	
	Semisolid	0	39	59	18	117	78	
	Solid	1	3	1	0	5	4	
	Formed	0	0	0	0	0	1	
	Total	10	60	62	19	151	151	
		Amount of zinc given						
	Consistency of stool	5mg	10mg	15 mg	20 mg	TotalT1	TotalT2	P- value
Day 7	Soft	7	2	0	0	9	15	0.412
	Semisolid	3	56	60	18	137	130	
	Solid	0	2	1	2	5	6	
	Watery	0	0	0	0	0	0	
	Mucoid	0	0	0	0	0	0	
	Total	10	60	61	20	151	151	

Table 4: Distribution of diarrhea 1 Patients according to the Consistency of stool.

Table 4 describes that On day 3, Ten Patients to whom 5-6mg treatment was given five of them had passed Watery stools, two passed soft stool, one passed Formed and two patients passed semi solid stool. Sixty patients were given 10 mg dosage in which 15 passed watery stool, 37 passed soft stool, 2 patients passed formed stool and 5patients passed semi solid stool. As P values of study were 0.001 and 0.000 at day 3 or day 5 are significant and at day 7 P-value is 0.412 which was not significant.

D I S C U S S I O N :

the control group had past history of diarrhea which necessitated hospital admission, the different is statically significant. P = < 0.05.Zinc deficiency may be an important underlying factor for recurrent diarrhea, which has important implication, as recurrent diarrhea is an established risk factor for malnutrition. Study conducted in Dashinpori, New Delhi in 1998, showed similar finding with P value of 0.002 which are consistent with zinc deficiency.

Most of case of diarrhea patients range under the age of 6 months. 96% of patients suffering from diarrhea were severely dehydrated of treatment group at the time of arrival. Of Control group 72% units were severely dehydrated. Hygiene conditions were the main factors for introducing diarrhea to the patient, most of the patients have the history of the poor hygiene e.g. they did not wash their hands eatable items. We have taken the history relating to washing of utensils eatable items, cleaning of area. Most of the patients have the history improper hygiene.

We have given our treatment to patients for ten days. We have calculated data on daily bases. But here we present data of patients of day 3, 5 and 7. Treatment of zinc we applied varies from 5mg to 20mg. we had checked frequency and consistency of stool.

If we see the results of our treatment and control group, frequency of stool pass at day 3 between 1-3 is found in one patient who had received 10mg of dosage. Control group had more frequency of stool pass. 82 patients who were passing 4-7 stools were given zinc in different dosage form. Similar frequency stool passing group were also given control treatment. Different dosage form of zinc for different frequency of stool passing had been given.

We used zinc supplement in different concentrations, for seven days to study the consistency of stool in diarrhea patients. Comparison of experimental and control group showed that zinc group with concentration 11-15mg had high recovery rate. Much of patients with zinc treatment have semi solid consistency within seven days. These results support our hypothesis that zinc have high recovery rate for treatment of diarrhea. It was clear in this study that, the mean reduction in number of watery stool was greater in zinc supplemental group as compared with control group. This

agreed with Saza well and the study done in Matab field which showed similar finding. Shanker A H, et al studies in Nepal, reported non significant difference in reduction of number of stool per day between the groups, which received zinc, and the control group. This finding was not agreement in this study.

Previous studies have demonstrated the effect of zinc supplementation on overall duration and frequency of stool passage. These findings were consistent with the finding of the study done by Ram, et al 2002 with P value of 0.001.Those who improved completely in zinc supplemented patient were zinc deficient (P<0.001). Children who had low zinc level on admission and received zinc supplementation had obvious improvement comparable with the place bo group (P=<0.001) This result agreed with work done in K.C.E.H showed similar findings. The findings of this study are in agreement with studies conducted in collaboration with the WHO, which recommended that children with acute diarrhea should be given zinc supplements. Mothers of children receiving zinc perceived earlier that the diarrhea had resolved. This is potentially of major clinical importance. The mothers in the study had a good 'feeling' about the medicines being given and were trying to guess the 'correct' medicine by looking at its effect on their neighbor's child.

C O N C L U S I O N :

The current study concluded that Zinc supplements given during diarrhea reduced the duration and severity of the condition. This research project showed significant reduction in frequency and consistency of stool per day as p value less than 0.05. Children who received 15 mg/day Zinc Supplementation showed a marked improvement in all outcome measures, suggesting that this deficiency is amendable to correction by replacement. The main predisposing factors for diarrhea were poor nutritional history with low intake of foods rich in zinc, in adequate feeding during illnesses, in adequate breast feeding and poor social class. T1 number of Patients improved from treatment were 140 and not improved patients were 11. In T2 improved from treatment were 132 and not improved patients were 19.

R E F E R E N C E S :

[1] Santosham M, Chandran A, Fitzwater S, Fischer-Walker C, Baqui AH, Black R. Progress and barriers for the control of diarrheal disease. The Lancet. 2010; 376(9734):63-7. doi.org/10.1016/S0140-6736(10)60356-X

[2] Motamed F, Kazemi N, Nabavizadeh R. Assessment of chronic diarrhea in early infancy in Tehran Tertiary Care Center; Tehran-Iran. Int. J. Pediat. 2015;3(2.1):4550.http://libmast.utm.my/Record/doaj-art-ac10f966edeb497996a4c6723814eea7

[3] Mushtaq I, Cheema HA, Malik HS, Waheed N, Hashmi MA. Causes of chronic non-infectious diarrhea in infants less than 6 months of age: rarely recognized entities. J. Ayub Med. Coll., Abbottabad: JAMC. 2017; 29(1):78-82. https://pubmed.ncbi.nlm.nih.gov/28712180/

[4] Abubakar I, Tillmann T, Banerjee A. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015; 385 (9963):117-71. doi.org/10.1016/S0140-6736(14)61682-2

[5] Fine KD, Schiller LR. AGA technical review on the evaluation and management of chronic diarrhea. Gastro enterology. 1999; 116(6):1464-86. doi.org/10.1016/S0016-5085(99)70513-5

[6] Hasan MM, Richardson A. How sustainable household environment and knowledge of healthy practices relate to childhood morbidity in South Asia: analysis of survey data from Bangladesh, Nepal and Pakistan. BMJ Open. 2017; 7(6):e015019. doi.org/10.1136/bmjopen-2016-015019

[7] Schertzer KA, Garmel GM. Acute Infectious Diarrhea. Emergency Management of Infectious Diseases.2018:169.doi.org/10.1017/9781316597095.027

[8] Prasad AS. Discovery of human zinc deficiency: its impact on human health and disease. Advances innutrition.2013;4(2):17690.doi.org/10.3945/an.112.003210

[9] RichardsL, Claeson M, Pierce NF. Management of acute diarrhea in children: lessons learned. The Pediatric Infectious disease J. 1993; 12(1):5-9. doi.org/10.1097/00006454-199301000-00003

[10] 1Harris S, Black RE. How useful are pharmaceuticals in managing diarrheal diseases in developing countries? Health policy and planning. 1991; 6(2): 141-7. doi.org/10.1093/heapol/6.2.141

[11] Walker CLF, Fontaine O, Young MW, Black RE. Zinc and low osmolarity oral rehydration salts for diarrhea: are newedcallto action. Bulletin of the World Health Organization. 2009; 87:780-6. doi.org/10.2471/BLT.08.058990

[12] Nout M, Motarjemi Y. Assessment of fermentation as a household technology for improving food safety: a joint FAO/WHO workshop. Food Control. 1997; 8(5-6): 221-6. doi.org/10.1016/S0956-7135(97)00021-2

[13] Barrell R, Rowland M. Infant foods as a potential source of diarrheal illness in rural West Africa. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1979; 73(1): 85-90. doi.org/10.1016/0035-9203(79)90136-6

[14] Bui QT-T, Lee H-Y, Le AT-K, Van Dung D, Vu LT-H. Trends and determinants for early initiation of and exclusive breast feeding under six months in Vietnam: results from the Multiple Indicator Cluster Surveys, 2000-2011.Global Health Action. 2016; 9(1): 29433. doi.org/10.3402/gha.v9.29433

[15] Yamamoto D, Ghosh S, Kuzuya M,Wang Y-H, Zhou X, Chawla-Sarkar M, etal. Whole-genome characterization of human group C rota viruses: identification of two line ages in the VP3 gene. J. General. Virology.2011; 92(2):361-9.doi.org/10.1099/vir.0.027375-0

[16] Alam M, Alam M, Nahar A, Kobayashi N. Molecular epidemiological studies on rota virus infection causing severe diarrhea in human, animals and poultry. Bangla. J. Veter. Med. 2011; 9(2): 167-75. doi.org/10.3329/bjvm.v9i2.13473

[17] Lanz Uhde F, Kaufmann T, Sager H, Albini S, Zanoni R, Schelling E, etal. Prevalence off our enteropathogens in the faeces of young diarrhoeic dairy calves in Switzerland.Veterinary Record. 2008;163(12):362-6.doi.org/10.1136/vr.163.12.362

[18] Bhandari N, Bahl R, Taneja S, Strand T, Molbak K, Ulvik RJ, et al. Effect of routine zinc supplementation on pneumonia in children aged 6 months to 3 years: randomized controlled trial in a nurbanslum. BMI. 2002;324(7350):1358.doi.org/10.1136/bmj.324.7350.1358

[19] Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. The Ame.J.ofclinicalnutrition.2000;72(6):1516-22.doi.org/10.1093/ajcn/72.6.1516

[20] World Health Organization, Research SPf, Diseases TiT, Diseases WHO DoCoNT, Epidemic WHO, Alert P. Dengue: guidelines for diagnosis, treatment, prevention and control: World Health Organization; 2009.

[21] Oberleas D, Harland B. Nutritional agents which affect metabolic zinc status. Progress in clinical and biologicalresearch.1977;14:1127.https://pubmed.ncbi.nlm.nih.gov/203946/

[22] Markowitz ME, Rosen JF, Mizruchi M. Circadian variations in serum zinc (Zn) concentrations: correlation with blood ionized calcium, serum total calcium and phosphate in humans. Ame. J. Clin. Nutr.1985;41(4):689-96.doi.org/10.1093/ajcn/41.4.689

[23] Soncin F, Guitton J-D, Cartwright T, Badet J. Interaction of human angiogenin with copper modulates angiogenin binding to endothelial cells. Biochemical and biophysical research communications.1997;236(3):604-

10. doi.org/10.1006/bbrc.1997.7018

[24] OuyangY, MaH, JinM, WangX, WangJ, XuL, etal. Etiology and epidemiology of viral diarrhea in children under the age of five hospitalized in Tianjin, China. Archives of Virology. 2012;157(5):881-7. doi.org/10.1007/s00705-012-1235-9