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ORIGINAL ARTICLE

Decrease in Stool Frequency with Zinc Supplementation in Acute Watery Diarrhea

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ABSTRACT

Objective: To compare mean decrease in stool frequency in patients with zinc supplementation versus placebo in addition to ORS in children with acute diarrhea.

Study Design: Randomized control study

Place and Duration of Study: The study was held at diarrhea ward of the Institute of Child Health and Children's Hospital Lahore from 15 March to 15 September, 2017.

Material and Methods: Inclusion criteria was children age 6 months to 5 years with duration of diarrhea <3 days. An informed consent was taken. Group A was considered as zinc supplemented group and given syrup zinc sulfate 20 mg/day plus ORS while group B as placebo group and was given ORS and placebo dextrose saline solution 20 ml daily. Final outcome was measured on day 7 by determining the decrease in stool frequency in zinc group as compared to placebo.

Results: Amongst 150 cases, in Zinc and Placebo group mean duration of diarrhea was 7.75 ± 4.19 days and 8.87 ± 3.78 days respectively with same mean duration, p-value >0.05. After treatment (7th day), mean decrease in frequency of stool was significantly high in Zinc group (8.20 ± 4.13) when compared to placebo group (3.15 ± 4.47), p-value <0.001.

Conclusion: Amongst children, supplementation of zinc with addition of ORS results in reduction of frequency of stools so zinc can significantly reduce the diarrhea and its complications.

Key Words: Zinc, Diarrhea, ORS.

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INTRODUCTION

Globally, diarrhea is still the most common pediatric morbidity, with 1.5 billion episodes and almost two million deaths per year.¹ It refers to an increased frequency of stools or the passage of loose or watery stools for the child, can lead to dehydration, which alters the child's natural balance of electrolyte (sodium, potassium, chloride) and to water, imbalance. If not treated promptly, it can be serious. Zinc is a constituent of more than one hundred metalloenzymes and is

essential for epithelial repair, growth, synthesis of DNA and RNA in cells and protein synthesis.² Endogenous intestinal excretion of zinc changes seems to be more important than changes in absorptive efficiency for maintenance of zinc homeostasis.³ In acute diarrhea, daily losses of zinc in intestinal fluid are as high as 159 microgram per kg per day as compare to 47 microgram per kg per day in normal children. Zinc deficiency leads to skin lesion, diarrhea, growth retardation, alopecia, delayed bone maturation, reduced appetite and because of defects in

immune system, there is increased susceptibility to infection especially amongst children and infants.⁴ It also has direct effect on gastro intestinal tract integrity via alteration in immune function that leads to increased clinical severity and duration of diarrhea.⁵ Possible mechanism for zinc treatment effect on diarrhea include increased absorption of water and electrolytes by intestine, increased level of enterocyte brush border enzymes, faster regeneration of gut epithelium and enhance immune response leading to early clearance of diarrheal pathogen from intestine.⁶ In treatment of persistent diarrhea, zinc is mostly used, while more research is needed on the use of zinc supplementation in treatment of acute diarrhea, a study conducted locally which included malnourished and immune compromised children as well.³ We want to see the effect of supplementation of zinc on healthy children (non-immune compromised) in terms of reduction in severity and duration of diarrhea. To reduce the now common treatment of diarrhea with unnecessary antibiotics and anti-diarrheal, the use of effective and inexpensive nutrient supplement would be helpful. So it has been planned to conduct a study to determine effectiveness of zinc supplementation in children with acute diarrhea in terms of reduction in frequency of loose stools.

MATERIAL AND METHODS

It was a randomized control study held at the diarrhea ward of emergency department of the Children's Hospital and the Institute of Child Health, Lahore from 15 March to 15 September 2017. The criteria of inclusion was children age between six months to five years of both genders with duration of diarrhea less than fourteen days at presentation. Patients having chronic diarrhea (diarrhea lasting for more than 14 days), bloody diarrhea, malnourished and immune compromised were excluded. Sample size of 150 cases (75 in each group) is calculated with 95% confidence level, 80% power of test and taking expected mean \pm S.D of mean decrease in stool frequency on 7th post treatment day i.e. 9.3 ± 2.49 VS 3.88 ± 2.45 in placebo VS Zinc group. Non Probability consecutive sampling technique was used. After taking ethical clearance a total number of 150 patients fulfilling inclusion criteria were taken from diarrhea ward of emergency of Institute of Child Health and Children's Hospital Lahore. An informed consent was taken from the parents prior to enrolment in the study. The attendant of patient

was requested to pick one of two cards randomly and this patient was allocated a group according to card A or B. Patients with card A were labeled as zinc supplemented group while patients with card B as non-zinc supplemented group.

The process was continued till sample size is completed with 50% patients in group A and 50% patients in group B. After initial rehydration and stabilization, group A was given syrup zinc sulfate 20 mg per day plus ORS while group B was given ORS and placebo dextrose saline solution 20ml daily. Then final outcome was measured on day 7 by determining the decrease in stool frequency in zinc group as compared to placebo. Data was entered in Performa. The collected data was analysed statistically by using SPSS version 16. Quantitative variables like age, Weight, decrease in frequency of stool pre and post- treatment was presented in form of mean \pm S.D. Qualitative variables like gender was presented in form of frequency and percentage. Test was used to compare the decrease in frequency of stools in both groups. Data was stratified for age, gender, duration of diarrhea, frequency of stool at admission to deal with effect modifiers. Post stratification t-test was applied. P-value ≤ 0.05 was considered as significant.

Operational definitions

Acute watery diarrhea: Acute diarrhea is defined by the World Health Organization (WHO) as the passage of three or more loose or liquid stools per day, for three or more days, and for less than 14 days.⁷

Decrease in stool frequency: Stool frequency was measured on history as number of stools/day on 7th day of treatment and was subtracted from stool frequency before treatment.

RESULTS

Amongst 150 cases, 80 (53.3%) were male and 70 (46.7%) were female. In Zinc group there were 37 (49.3%) female and 38 (50.7%) were male patients while in placebo group there were 42 (56%) male and 33 (44%) were female patients. Over all mean age of patients was 1.59 ± 1.27 years. In Zinc group mean age of patients was 1.78 ± 1.36 years and in placebo group the mean age of patients was 1.41 ± 1.17 years. The mean age in both groups was statistically same, p-value

>0.05. (table 1). Average weight in Zinc group and Placebo group was statistically same, i.e. 9.01 ± 3.33 kg and 8.77 ± 3.30 kg respectively, p-value >0.05 (fig 1). In Zinc and Placebo group mean duration of diarrhea was 7.75 ± 4.19 days and 8.87 ± 3.78 days respectively with same mean duration, p-value >0.05. Before treatment mean number of stool in Zinc and placebo was 12.12 ± 4.03 and 11.67 ± 2.85 with insignificant difference, p-value >0.05. After treatment (7th day) mean number of stools were significantly less in Zinc group (3.92 ± 1.50) when compared to placebo group (8.16 ± 3.87), p-value <0.05. Mean decrease in frequency of stool was significantly high in Zinc group (8.20 ± 4.13) when compared to placebo group (3.15 ± 4.47), p-value <0.001 (table 2). Comparison of Stool frequency in both study groups with respect to age groups is shown in fig 2.

TABLE 1: Comparison of age (years) in both study groups

		N	Mean	S.D	p-value
Age (years)	Zinc group	75	1.78	1.36	0.076
	Placebo	75	1.41	1.17	
	Total	150	1.60	1.28	

TABLE 2: Comparison of Stool frequency in both study groups

		N	Mean	S.D	p-value
Stool frequency at admission	Zinc group	75	12.12	4.03	0.428
	Placebo	75	11.67	2.85	
	Total	150	11.89	3.49	
Stool frequency at 7 th day	Zinc group	75	3.92	1.50	<0.001
	Placebo	75	8.16	3.87	
	Total	150	6.04	3.62	
Decrease in stool	Zinc group	75	8.20	4.13	<0.001
	Placebo	75	3.51	4.47	
	Total	150	5.85	4.89	

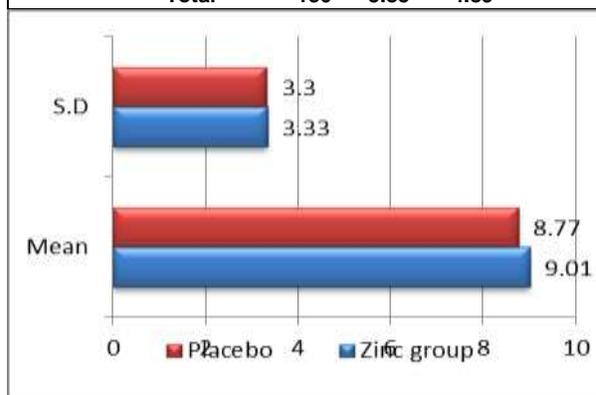
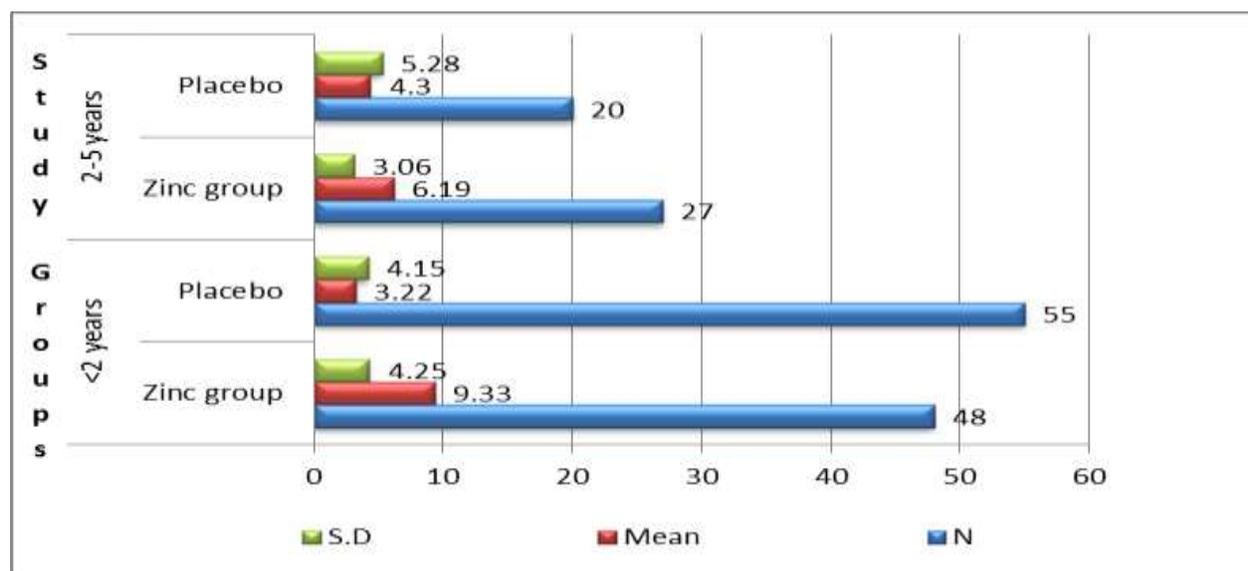


Fig 1: Comparison of weight (kg) in both study groups



P value: Less than 2 years: <0.001 2-5 years: 0.130

Fig 2: Comparison of stool frequency in both study groups with respect to age groups

DISCUSSION

In children <5 years, gastroenteritis is a common cause of death in developing countries. While deaths from diarrhea are less common in developed countries, much illness leads to doctor visits or hospitalization.⁸ WHO currently recommends zinc supplementation and early oral rehydration therapy for treating diarrhea in children between 6 and 60 months of age.⁹ Amongst children, for the treatment of diarrheal episodes, zinc supplementation is a critical intervention. In children with acute diarrhea, the World Health Organization (WHO) and UNICEF recommend 10 – 14 days of zinc supplements in a dose of 20 mg per day, and 10 mg per day for infants under six months old, to decrease the severity of the episode and prevent further occurrences.¹⁰ According to Pakistan Health Survey (2012), only 2% of children were receiving zinc for diarrhea, which only increased to 8% in the 2017-2018 survey.^{11,12} Furthermore, according to the National Nutrition Survey 2011, 39.2% of Pakistani children of ages zero to five years were zinc deficient.¹³ A study done by Walker et al who showed preponderance of female¹⁴ while in our study, males were predominant. A multi-centric study reported mean age of patients treated with zinc and placebo was 97.8 ± 43.0 days and 99.2 ± 41.5 days, while in our study was 1.59 ± 1.27 years. A study reported that the frequency of mean diarrhea (4.5 ± 2.3 vs. 5.3 ± 2.1 ; $p=0.004$) was less in the group receiving ORS plus zinc¹⁵ while in our study, insignificant difference was observed in mean number of stools before and after treatment in both groups. A pooled analysis of four RCTs has been reported in less than 5 years of children with diarrhea, on the effects of oral zinc supplements and to evaluate the overall effect of zinc on the continuation of diarrhea, the Cox survival regression analysis was used. Zinc-supplemented children with persistent diarrhea had a 24% lower probability of continuing diarrhea (95% CI: 9%, 37%) and a 42% lower rate of treatment failure or death (95% CI: 10%, 63%) than those in the control group.¹⁶ In our study regarding reduction in stool frequency we found that after treatment (7th day) mean number stool was significantly less in Zinc group (3.92 ± 1.50) when compared to placebo group (8.16 ± 3.87), p -value <0.05 . Mean decrease in frequency of

stool was significantly high in Zinc group (8.20 ± 4.13) when compared to placebo group (3.15 ± 4.47), p -value <0.001 . A study reported no significant difference in mean decrease in frequency of stool in both groups, i.e. 5.0 ± 2.3 in zinc and 5.0 ± 2.4 in placebo, p -value that is a clear contradiction to our study¹⁴ as we found significant mean decrease in stool frequency at 7th day of treatment. One study conducted in Iran in 2013 showed that diarrhea frequency (4.5 ± 2.3 vs. 5.3 ± 2.1 ; $p=0.004$) was lower in the group receiving zinc +ORS as compared to ORS only group; however, the qualitative assessment of stool consistency also confirmed earlier improvement in the treatment group in the first three days of hospitalization ($p <0.05$). The mean duration of hospitalization was significantly lower in the patients receiving zinc supplements (2.5 ± 0.7 vs. 3.3 ± 0.8 days; $p=0.001$).¹⁷ These findings are supportive by current study. A local study conducted in Islamabad showed that the frequency of stools in Placebo group patients was reduced from 16.1 ± 4.48 stools/day to 6.80 ± 1.99 stools/day and in ZINC group from 15.66 ± 4.24 to 1.78 ± 1.79 stools/day.³ Study concluded that ZINC has no effect on acute diarrhea. That is a contradiction with our study. In 40 infants (6 - 18 months old) with persistent diarrhea (greater than two weeks' duration), an RCT evaluated the effect of oral zinc supplementation and revealed that there was depletion of zinc in persistent diarrhea with the progression of the illness, and the zinc status was improved by oral zinc administration.¹⁸ In current study when data was stratified over age groups, gender, duration of diarrhea and frequency of stool at admission, we found significant higher mean decrease in frequency of stool in zinc group, p -value <0.05 , other than age group of 2-5 years of age, p -value >0.05 . The higher age groups may not show better outcome using zinc supplements to reduce frequency of diarrhea.

CONCLUSION

Amongst children in this study, supplementation of zinc with addition of ORS results in reduction of frequency of stools so zinc can significantly reduce the diarrhea and its complications.

Conflict of interest: Nil

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REFERENCES

1. Laghari GS, Hussain Z, Shahzad H. Effect of Zinc Supplementation on the Frequency and Consistency of Stool in Children with Acute Diarrhea. *Cureus* 2019;11(3): e4217.
2. Sazawal S, Black RE, Bhan MK, Bhandari N, Sinha A, et al. Zinc supplementation in young children with acute diarrhea in India. *New England Journal of Medicine* 1995;333(13):839-44.
3. Choudhry S, Tariq PA, Afzal A. Zinc Supplementation in Children with Acute Diarrhea. *Journal of Rawalpindi Medical College (JRMC)* 2009;13(2):66-9.
4. Sazawal S, Black R, Bhan M, Jalla S, Sinha A, et al. Efficacy of zinc supplementation in reducing the incidence and prevalence of acute diarrhea--a community-based, double-blind, controlled trial. *The American journal of clinical nutrition* 1997; 66 (2):413-8.
5. Kosek M, Bern C, Guerrant RL. The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. *Bulletin of the World Health Organization* 2003;81(3):197-204.
6. Patel AB, Dhande LA, Rawat MS. Therapeutic evaluation of zinc and copper supplementation in acute diarrhea in children: double blind randomized trial. *Indian pediatrics*. 2005;42(5):433-42.
7. WHO. The treatment of diarrhoea: a manual for physicians and other senior health workers. In: Organization WH, editor. 2005
8. Glass RI, Bresee J, Jiang B, Gentsch J, Ando T, Fankhauser R, et al., editors. *Gastroenteritis viruses: an overview*. Novartis Foundation Symposium; 2001: Chichester; New York; John Wiley; 1999.
9. Galvao TF, Pontes RF, Silva MT, Pereira MG. Zinc supplementation for treating diarrhea in children: a systematic review and meta-analysis. *Revista panamericana de salud publica*. 2013;33(5):370-7.
10. Bajait C, Thawani V. Role of zinc in pediatric diarrhea. *Indian Journal of Pharmacology*. 2011;43(3):232-5.
11. Pakistan demographics and health survey. Dec;2018; <http://nhsrc.pk/dashboards/indicatorselect.php?target=pdhs&years=2012-13> 2013.
12. Available from; [Dec;2018]. 2018. Pakistan demographics and health survey.
13. Pakistan National Nutrition Survey 2011. UNICEF Pakistan. [Feb;2019]; <https://www.mhinnovation.net/sites/default/files/downloads/innovation/research/Pakistan%20National%20Nutrition%20Survey%202011>.
14. Bajait C, Thawani V. Role of zinc in pediatric diarrhea. *Indian Journal of Pharmacology*. 2011;43(3):232-5.
15. Walker CLF, Bhutta ZA, Bhandari N, Teka T, Shahid F, Taneja S, et al. Zinc supplementation for the treatment of diarrhea in infants in Pakistan, India and Ethiopia. *Journal of pediatric gastroenterology and nutrition*. 2006;43(3):357-63.
16. Karamyyar M, Gheibi S, Noroozi M, Kord Valeshabad A. Therapeutic Effects of Oral Zinc Supplementation on Acute Watery Diarrhea with Moderate Dehydration: A Double-Blind Randomized Clinical Trial. *Iranian Journal of Medical Sciences*. 2013;38(2):93-9.
17. Bhutta ZA, Bird SM, Black RE, Brown KH, Gardner JM, Hidayat A, et al. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. *The American journal of clinical nutrition*. 2000;72(6):1516-22.
18. Karamyyar M, Gheibi S, Noroozi M, Valeshabad AK. Therapeutic effects of oral zinc supplementation on acute watery diarrhea with moderate dehydration: a double-blind randomized clinical trial. *Iranian Journal of Medical Sciences* 2013; 38 (2):93-9.