

Comparison of Mean Change in Frequency of Stool with Zinc Supplementation versus Placebo in Children with Acute Diarrhoea

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Abstract

Objective: To determine the effect of zinc supplementation in children with watery diarrhoea. The objective was to compare the mean change in frequency of stool with zinc supplementation versus placebo in paediatric patients with acute diarrhoea in addition to standard treatment.

Method: It was a randomized controlled study done in Department of Paediatrics, Punjab Rangers Teaching Hospital, Lahore over 6 months. 68 children of both genders aged under 5 years who presented with acute diarrhoea were sub-divided into two equal groups; Group -A received oral zinc with standard management while those in Group-B received standard management alone. Frequency of stools was recorded after 72 hours, mean change calculated and then compared between the groups.

Results: Mean duration of acute diarrhoea was 3.81 ± 1.56 days. The study groups were comparable with regards to mean frequency of stools at presentation (7.71 ± 2.76 vs. 7.79 ± 2.67 ; p -value=0.894). However, after 72 hours, the mean frequency of stools was significantly lower in children receiving additional zinc supplementation as compared to placebo (3.94 ± 2.84 vs. 5.50 ± 2.77 ; p -value=0.025). The mean change in the frequency of stools was considerably higher in the group on zinc supplementation as compared to placebo group (3.76 ± 0.89 vs. 2.29 ± 0.63 ; p -value<0.001).

Conclusion: In this study, zinc supplementation was found superior to conventional management of children presenting with acute diarrhoea evident from considerably greater reduction in the mean frequency of stools. The low cost, wide-spread availability and ease of administration advocate the preferred use of zinc in the management of such patients.

Key Words: Acute Diarrhoea, Zinc Supplementation, Loose Stools

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Introduction

Diarrheal diseases is one of the most common cause of morbidity around the world and is the second highest reason of deaths in children, aged one month and above, after pneumonia. Annually, it accounts for more than 1 million deaths, with most occurring in deve-

loping countries. Therefore, 25% of deaths in young children living in South-East Asia are attributed to acute watery diarrhoea.¹ In spite of improvements in standard of living, advancement in water purification, food hygiene and sanitation, diarrheal disease remains a significant economic burden.²

Zinc deficiency, which is a major part of malnutrition, is associated with growth restriction and increased incidence of diarrhoea and pneumonia, especially in children <5 years of age. Around the world, zinc deficiency is responsible for around 170,000 deaths from diarrhoea and 400,000 deaths from acute respiratory illnesses in the same age group, which accounts for 4% of mortality.³⁻⁵ An Indian study by Sachdev et al. on a trial of zinc supplementation in children admitted to

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hospital with acute gastroenteritis, reported similar findings.⁶

Zinc is of considerable importance to public health, as it is necessary for strengthening of immune system and growth. It also plays a role in improving intestinal function and optimal development of brain.⁷ There is an increased risk and severity of infectious diseases, such as, AGE (acute gastroenteritis) and ARI (Acute respiratory Infections) in children with under-nutrition and accounts for 35% mortality.⁸

Supplementation with zinc reduced fecal output in children with deficiency and many clinical trials confirmed an improvement with zinc supplements AGE. An analytical study conducted by Chirla S et al. came to the conclusion that, with zinc supplementation, there was a 15% lower probability of continuation of diarrhoea in acute cases and 24% lower probability in persistent cases (>14 days).⁹ The large number of cases of diarrhoea in resource-limited countries is associated with lack of access to clean drinking water, improper sanitation, and poor health and nutrition.¹⁰ In a study, children who received zinc reported 12.5% reduction in stool frequency, 15.5% shortening of diarrhoea duration, and 18.0% reducing diarrhoea.¹¹

There are limited local studies on zinc supplementation in children with diarrhoea. If we are able to prove the role of zinc supplementation in children with diarrhoea, it will not only fill the knowledge gap but also will help in treating the dehydration in our children in better way and reduction in morbidity and mortality due to diarrhoea. Therefore, this study has been planned to determine the effect of zinc supplementation in children with watery diarrhoea. The objective was to compare the mean change in frequency of stool with zinc supplementation versus placebo in paediatric population with acute gastroenteritis in addition to standard treatment.

Material and Method

A randomized controlled study was performed at the Department of Paediatric Medicine, Punjab Ranger's Teaching Hospital Lahore over 6 months from 25/01/2021 to 24/07/2021. A total of 68 (34 in each group) patients were taken in this study, the sample size was estimated

at 80% power of test and 95% confidence level and the mean change in stool frequency at 72 hours was expected as 3.74 ± 0.17 with zinc supplementation and 2.09 ± 2.7 with placebo, in children with acute diarrhoea.

Selection of patients was by consecutive, non-probability sampling. The inclusion criteria were all children, between 2 months to 5 years of age with acute watery diarrhoea. The definition of acute watery diarrhoea is the passage of 3 or more stools per day, of consistency grade III or more (grading given in annexure), of duration of no longer than 14 days. Children excluded from the study were those with 3rd degree malnutrition, severe dehydration, systemic infection, blood in stools and other comorbidities.

All information was recorded on a structured questionnaire. All selected cases were given a probiotic and oral rehydration solution. In addition, a light diet was given to children who were able to take solids. The lottery method was used to divide the sample into two groups.

The first group (n=34) was given zinc supplementation by a staff nurse in addition to the regime mentioned above; the second group did not receive additional zinc supplementation. Outcome was derived on the basis of assessment of improvement in the condition of the patient. For infants <6 months of age, 10 mg/day zinc was prescribed, and for >6 months group, 20 mg/day zinc was given. Documentation of age, gender, the duration of diarrhoeal symptoms and the type of milk feed (breast milk vs. formula) was taken. On Day-1, notes were taken on the number of diarrhoea episodes and stool consistency, then repeated on Day-3. Outcome was measured, as change in frequency of stool, at 72 hours, in terms of mean change in number of stools passed. Then number of stools were noted after 72 hours of giving zinc supplementation. The number of stools at admission and at 72 hours was subtracted for change. Patients were followed up in wards. The data was analyzed through SPSS version 25.0.

Results

Selected cases ages were from 6 to 60 months with a mean of 25.3 ± 14.7 months. Majority (n=30, 44.1%)

of the children were aged above 2 years (Fig 1.). There were 41 (60.3%) boys and 27 (39.7%) girls with boys to girls ratio of 1.5:1 (Fig 2) The number of days that acute diarrhoea remained ranged from 2 to 7 with a mean of 3.81 ± 1.56 days.

Both the study groups were comparable in terms of mean age (p-value=0.954), mean duration of diarrhoea (p-value=0.700) and duration of diarrhoea (p-value=0.806) as shown in Table 1.

The frequency of stools ranged from 3 to 12 at presentation with a mean of 7.75 ± 2.70 while 0 to 11 after 72 hours of treatment with a mean of 4.72 ± 2.89 . The change in frequency of stools ranged from 1 to 5 with a mean of 3.03 ± 1.07 . Both groups were comparable in terms of mean frequency of stools at presentation (7.71 ± 2.76 vs. 7.79 ± 2.67 ; p-value=0.894). However, after 72 hours, the mean frequency of stools was significantly lower in children receiving additional zinc supplementation as compared to placebo (3.94 ± 2.84 vs. 5.50 ± 2.77 ; p-value=0.025). The mean change in the frequency of stools was significantly higher in the zinc group as compared to placebo group (3.76 ± 0.89 vs. 2.29 ± 0.63 ; p-value<0.001) (Table 2). A similar difference was noted in mean change in frequency of stools between the groups based on age, gender and duration of diarrhoea as shown in Table 3.

Table 1: Baseline Characteristics of Study Groups n=68

Characteristics	Zinc n=34	Placebo n=34	P-value
Age (months)	25.4 ± 15.7	25.2 ± 13.9	0.954
• ≤ 1 years	7 (20.6%)	6 (17.7%)	0.943
• 1-2 years	12 (35.3%)	13 (38.2%)	
• 2-5 years	15 (44.1%)	15 (44.1%)	
Gender			
• Boys	21 (61.8%)	20 (58.8%)	0.804
• Girls	13 (38.2%)	14 (41.2%)	
Duration of Diarrhoea (days)	3.74 ± 1.68	3.88 ± 1.45	0.700
• 2-4 days	19 (55.9%)	20 (58.8%)	0.806
• 5-7 days	15 (44.1%)	14 (41.2%)	

Chi-square test and independent sample t-test, observed difference was statistically insignificant

Discussion

Acute gastroenteritis remains a major source of ill-

health and morbidity in children under 5 years in countries with limited resources. This massive burden accounts for 800,000 child deaths, annually, from diarrhoea in the preschool age group, which translates into more than 10% of total paediatric deaths.² Bringing down these numbers is vital to reduce the child mortality rate by two-thirds until 2025, as planned by UN's Millennium Development Goal 4.^{1,2,12}

Zinc is a potent agent in the intestine by modulating ion transport, stimulating enterocyte growth and differentiation, decreasing intestinal permeability, and regulating oxidative stress and inflammation.³ Intestinal loss in acute diarrhoea leads to zinc deficiency, and chronic

Table 2: Comparison of Means of Frequency of Stools before and after the Treatment as well as Mean Change between the Study Groups n=68

Frequency of Stools per Day	Zinc n=34	Placebo n=34	P-value
At Presentation	7.71 ± 2.76	7.79 ± 2.67	0.894
After 72 hours	3.94 ± 2.84	5.50 ± 2.77	0.025*
Mean Change	3.76 ± 0.89	2.29 ± 0.63	<0.001*

Independent sample t-test, * observed difference was statistically significant

Table 3: Comparison of Mean Change in the Frequency of Stools between the Study Groups n=68

Subgroups	Mean Change in Frequency of Stools		P-value
	Zinc n=34	Placebo n=34	
Age			
• ≤ 1 years	3.71 ± 0.76	2.33 ± 0.52	0.003*
• 1-2 years	3.83 ± 1.03	2.31 ± 0.63	<0.001*
• 2-5 years	3.73 ± 0.88	2.27 ± 0.70	<0.001*
Gender			
• Boys	3.76 ± 0.89	2.30 ± 0.57	<0.001*
• Girls	3.77 ± 0.93	2.29 ± 0.73	<0.001*
Duration of Diarrhea			
• 2-4 days	3.79 ± 0.98	2.35 ± 0.67	<0.001*
• 5-7 days	3.73 ± 0.80	2.21 ± 0.58	<0.001*

Independent sample t-test, * observed difference was statistically significant

zinc deficiency makes the child more vulnerable to diarrhoea, leading to a vicious cycle.⁴ It has been seen in recent evidence that zinc supplementation has significant

benefit on the clinical course of acute diarrhoea by reducing the frequency of stools and duration of stay in hospital.¹³

In the current study, we observed that the mean age of children with acute gastroenteritis was 25.3±14.7 months. Our observation matches with that of Laghari et al. (2019) who reported a similar value of 25.12±6.05 months among such children presenting at Liaquat University of Medical and Health Sciences in Jamshoro.¹³ In another local study involving children with acute watery diarrhoea presenting at Combined Military Hospital (CMH) Peshawar, Ehsan et al. observed a mean age of 25.8±4.2 months.¹⁴ This was again echoed in an Indian study, by Mujawar et al. reporting a mean age of 27.1±10.2 months.¹⁵ Pickering et al. and Sarker et al. made a similar observation in Bangladesh and reported a comparable mean age of 29.3±16.7 months and 23.2 ± 3.2 months respectively in such children.^{16,17} Sathiadas et al. reported a comparable mean age of 25.0±12.1 months in Sri Lankan children with acute diarrhoea.¹⁸ Strand et al. reported a similar mean age of 25.9±7.2 months among Norwegian children presenting with diarrhoea,¹⁹ while Dhingra et al. reported it to be 23.2±15.3 months in Tanzania.²⁰

In the present study, we observed a relative male predominance among such children with boys to girls ratio of 1.5:1. Similar findings were seen in Laghari et al. who observed a male predominance of 1.5:1 among such children presenting at Liaquat University of Medical and Health Sciences, Jamshoro.¹³ Ehsan et al. observed similar male predominance (M:F; 1.6:1) among children with acute watery diarrhoea presenting at Combined Military Hospital (CMH) Peshawar¹⁴ while Qureshi et al. reported it to be 2.3:1 at Aga Khan University Hospital, Karachi.²¹ Mujawar et al. and Patel et al. reported similar male predominance among Indian such children with male to female ratio of 1.5:1 and 1.3:1 respectively^{15,22} while Palihawadana et al. reported it to be 1.5:1 in Sri Lanka.²³ Sobouti et al. observed similar male predominance in Iranian children with diarrhoea and reported it to be 1.6:1.²⁴

It was observed that after 72 hours of oral zinc supplementation, the mean frequency of stools was significantly lower in children receiving additional zinc as

compared to placebo (3.94±2.84 vs. 5.50±2.77; p-value = 0.025). Also, the mean change in the frequency of stools was significantly higher in the zinc group as compared to placebo group (3.76±0.89 vs. 2.29±0.63; p-value<0.001).

Our observation is in line with a similar previously published study where Laghari et al. evaluated the effect of zinc in the management of acute diarrhoea among children. They too reported that the mean frequency of stools after 72 hours of treatment was significantly lower in the experimental groups (2.40±0.81 vs. 4.28 ± 1.07; p-value<0.001) as compared to controls. They also observed a similar significantly greater reduction in the mean frequency of stools with zinc as compared to placebo (3.74±0.17 vs. 2.09±2.7; p-value<0.001).¹³

The addition of zinc was found superior to conventional management of children presenting with acute diarrhoea evident from considerably greater reduction in the mean frequency of stools regardless of child's age, gender and duration of diarrhoea which along with its low cost, wide-spread availability and ease of administration advocate the preferred use of zinc in the management of such children presenting in future paediatric practice so that the alarmingly high burden of diarrhoea and subsequent malnutrition in Pakistan can be reduced.

Conclusion

In the present study, addition of zinc was found superior to conventional management of children presenting with acute diarrhea evident from considerably greater reduction in the mean frequency of stools regardless of child's age, gender and duration of diarrhea which along with its low cost, wide-spread availability and ease of administration advocate the preferred use of zinc in the management of such children presenting in future pediatric practice.

Conflict of Interest:

None

Funding Source:

None

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Authors Contribution

MA: Conceptualization of Project

HA: Data Collection

SN: Literature Search

AQ: Statistical Analysis

MAK: Drafting, Revision

ZH: Writing of Manuscript