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Original Research Article

Compliance with 14 day zinc therapy for acute diarrhoea: a prospective observational study

Ajayprakash Veerapandiyan*, Deepti Pandit, Sujatha Sridharan, L. Umadevi

Department of Pediatrics, Chettinad Hospital and Research Institute, Chennai, Tamil Nadu, India

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***Correspondence:**
Dr. Ajayprakash Veerapandiyan,
E-mail: ajay.veera@icloud.com

ABSTRACT

Background: Acute diarrheal diseases remain a leading cause of global morbidity and mortality in young children. The effective implementation of provision of zinc in addition to low osmolarity ORS remains very poor.
Methods: A prospective observational study was done to determine compliance with zinc therapy on 103 children aged between two months to five years with acute gastroenteritis. They were started on WHO ORS and zinc in the form of syrup (20 mg/day in those >6 months of age and 10mg/day in those <6 months of age) and advised to continue for 14 days. Further episodes of diarrhea was considered as the primary outcome variable. Number of days zinc taken was considered as the primary explanatory variable. p-value <0.05 was considered statistically significant.
Results: The mean age was 19.49±14.41 months. The compliance to complete 14-day zinc therapy was 62.14%. The mean number of days zinc was taken was 11.28±3.81 days. In 11.65% of participants, there was further episodes of diarrhea. The main reasons for discontinuation were diarrhea stopped (45%), Ignorance (37.5%), URI (12.5%).
Conclusions: Findings indicate that the syrup formulation is acceptable, but further efforts are required to enhance adherence. These findings also highlight the importance of guiding in ensuring adherence to zinc duration while also addressing the tendency of caregivers to terminate treatment once a child appears to have recovered from an acute diarrheal episode.

Keywords: Acute diarrheal disease, Acute gastroenteritis, Compliance, World Health Organization - Oral rehydration solution, Young children, Zinc syrup

INTRODUCTION

Acute diarrheal diseases remain a leading cause of global morbidity and mortality particularly among young children in resource-limited countries.[1] In 2016, diarrhea was the fifth leading cause of death among children younger than 5 years and rotavirus was the leading etiological agent.[2] Acute diarrhea is one of the leading causes of childhood deaths despite the use of oral rehydration therapy (ORT).[1] On 8 May 2004, the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) recommended routine administration of zinc in the management of children, aged less than five years, with acute diarrhoea.[3] In making the recommendation, WHO and UNICEF also suggested careful monitoring for adverse events associated with the routine administration of zinc, particularly unusual or excess vomiting. Zinc supplementation is a critical new intervention for treating diarrheal episodes in children. Administration of zinc along with new low osmolarity oral rehydration solutions/salts (ORS), can reduce the duration and severity of diarrheal episodes for up to three months. The World Health Organization (WHO) and UNICEF recommend daily 20 mg zinc supplements for 14 days for children with acute diarrhea, and 10 mg per day for infants under six months old, to curtail the severity of the episode and prevent further occurrences in the ensuing -

two to three months, thereby decreasing the morbidity considerably. Zinc treatment is a simple, inexpensive, and critical new tool for treating diarrheal episodes among children.[4] Many countries have changed diarrhea management policies to include low osmolarity ORS and zinc, but there is a gap between policy change and effective program implementation, with very few children currently being appropriately treated.[5,6] Although the Government of India has initiated the provision of zinc in addition to low osmolarity ORS through the public health system, under the National Rural Health Mission, the acceptability of zinc and compliance to treatment is very poor. This study was primarily carried out to determine compliance with zinc therapy in children with acute gastroenteritis at 14 days. Secondary objectives included determining the causes for non - compliance with zinc therapy and comparing the recurrence of diarrhoea during 3 subsequent months in children with good compliance versus those with poor compliance. Information about the current acceptability of and compliance to zinc supplementation prescribed in the health facility among children (6 - 59 months old) with diarrheal illnesses, and the motivation of their mothers to administer the same consecutive 14 days, are lacking, especially in rural areas. The present study aims to determine the acceptability of and compliance zinc supplementation among children presenting with diarrhea to a tertiary care teaching hospital.

METHODS

A prospective observational study was done on 103 children aged between two months to five years in the pediatric department treated either as outpatient or inpatient with the Presence of loose stools with or without features of dehydration (acute gastroenteritis) after getting ethical clearance. The study was done from January 2019 till the required number of children are enrolled and their follow up is completed. A study done by Valekar SS showed compliance with 14-day zinc supplementation of 16% in Indian children. With an estimated prevalence of 16%, the absolute precision of 10%, the alpha error of 5, the required sample size was calculated to be 103 subjects. Children with pre-existing immunodeficiency, features of shock or systemic bacterial infection, diarrhoea lasting for >14 days at presentation were excluded. Enrolled children were started on WHO ORS and zinc in the form of syrup (20 mg/day in those >6 months of age and 10mg/day in those <6 months of age). Parents/ caregivers were counseled and advised to continue it for 14 days. They were followed up on day 5 and 10 through phone calls and on day 15 by follow up visit to the OPD and also at 3 months from the date of enrolment. Data was collected regarding the resolution of diarrhoea, duration of ORS and zinc supplementation. Further episodes of diarrhea was considered as the primary outcome variable. The number of days zinc taken was considered as the primary explanatory variable. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Non-normally distributed quantitative variables were summarized by the median and interquartile range (IQR). All Quantitative variables were checked for normal distribution within each category of an explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro- Wilk test was also conducted to assess normal distribution. Shapiro Wilk test p-value of >0.05 was considered as the normal distribution. Categorical outcomes were compared between study groups using Chi-square test /Fisher's Exact test (If the overall sample size was <20 or if the expected number in any one of the cells is <5, Fisher's exact test was used.) p-value <0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.[7]

RESULTS

A total of 103 subjects were included in the final analysis.

Table 1: Descriptive analysis of parameter in the study population.

Parameter	Summary
Gender N (%)	
Male	53 (51.46%)
Female	50 (48.54%)
Age in months (Mean±SD)	19.49±14.41
Weight in Kg (Mean±SD)	11.47±11.08
Taken for 14 days N (%)	
Yes	64 (62.14%)
No	39 (37.86%)
No of days Zn taken (Mean ± SD)	11.28±3.81
No of days Zn taken N (%)	
<5	10 (9.71%)
5 to 10	27 (26.21%)
>10	66 (64.08%)
Reason for discontinuation (N=40) N (%)	
Diarrhoea stopped	18 (45%)
Ignorance	15 (37.5%)
repeat diarrhea	1 (2.5%)
Unpalatable	1 (2.5%)
URI	5 (12.5%)
Further Episodes of Diarrhea (N=103) N (%)	
Yes	12 (11.65%)
No	91 (88.35%)

Among the study population, 53 (51.46%) participants were male and the remaining 50 (48.54%) participants were female. The mean age in months was 19.49±14.41. The mean of Weight in Kg was 11.47±11.08. out of 103 participant 64 (62.14%) were taken a zinc dose for 14 days. The mean number of days ZN taken was 11.28±3.81. 18 (45%) participants reason for discontinuation was diarrhea stopped, 15 (37.5%) participants reason for discontinuation was ignorance, 1

(2.5%) participant reason for discontinuation was repeated diarrhea, 1 (2.5%) participant reason for discontinuation was unpalatable and remaining 5 (12.5%) participant reason for discontinuation was URI. For 12 (11.65%) participants there was further episodes of diarrhea (N=103) (Table 1).

Among the study population, 2 (3.13%) participants had further episodes of Diarrhoea after 14 days of zinc therapy and the difference between two groups was statistically significant (p-value <0.001) (Table 2).

Table 2: Comparison of taken for 14 days between further episodes of diarrhoea (N=103).

Taken for 14 days	Further episodes of diarrhoea		Chi-square	Fisher exact p-value
	Yes	No		
Yes (N=64)	2 (3.13%)	62 (96.88%)	11.936	<0.001
No (N=39)	10 (25.64%)	29 (74.36%)		

Table 3: Comparison of no of days zinc taken between further episodes of diarrhoea (N=103).

No of days Zn taken	Further episodes of diarrhoea		Chi-square	p-value
	Yes	No		
<5 (N=10)	4 (40%)	6 (60%)	15.504	<0.001
5 to 10 (N=27)	6 (22.22%)	21 (77.78%)		
>10 (N=66)	2 (3.03%)	64 (96.97%)		

Among the study population for further episodes of diarrhoea 4 (40%) participants ZN was taken for less than 5 days, 6 (22.22%) participants ZN was taken for 5 to 10 days and 2 (3.03%) participants ZN was taken for less than 5 days, the and difference between the two groups was statistically significant (p-value <0.001) (Table 3).

DISCUSSION

Zinc is an essential trace element which has an important role in the normal functioning of the body and its enzyme systems. Marginal zinc deficiency is common in developing countries, particularly in children belonging to lower socioeconomic classes.[8] Administration of zinc along with new low osmolarity oral rehydration solutions/salts (ORS), can reduce the duration and severity of diarrheal episodes.[5,9,10] The possible mechanisms for the effect of zinc supplementation on diarrhea include improved intestinal absorption of water and electrolytes, quicker regeneration of the gut epithelium, increased levels of enterocyte brush border enzymes, and improved immune responses, leading to rapid clearance of pathogens causing diarrhoea from the intestine. Out of the 103 children included in the final analysis, 51.46% were male. The mean age of the study group was 19.49±14.41 months while the mean weight was 11.47±11.08 kg. Similar to this study, in the study by Lamberti LM et al, done in Uttar Pradesh, the mean age was 17.7 months and gender wise distribution (42.5% males) of study subjects was almost equal similar to this study.[11] But in their study, 89.3% of subjects took zinc tablets while 11.5% took zinc in the form of syrup. The mean number of days zinc was taken was 11.28±3.81 days in our study while in the study by Lamberti LM et al, it was 10.7 days.[11] The compliance to full zinc therapy of 14 days was 62.14% and similar to our study, Lamberti LM et al, reported that 47.8% continued treatment for the complete 14 days and they also observed that among children receiving zinc syrups and tablets respectively, the age-appropriate dose was received by 30.8% and 67.3%.[11]

Ahmed S et al, in their study observed that 62% of the children completed a full 10-day course of zinc treatment by taking one tablet a day that had been completely dissolved in a small amount of water (good compliance).[9] There was 63% excess risk for poor compliance to zinc if father stays at home with the family [OR = 1.63 (95%CI; 1.09, 2.46) p = 0.019] in their study. Despite vomiting, 33% children continued to receive zinc supplements [OR = 0.67 (95%CI; (0.47, 0.97, 0.032)] after adjusting for covariates. Both acceptability and compliance to dispersible zinc supplements in childhood diarrheal illnesses were still not at the expected level in rural Bangladesh in their study.[9] In this study, in 10(9.71%) participants zinc was taken for less than 5 days, in 27 (26.21%) participants zinc was taken for 5 to 10 days and for 66(64.08%) participants zinc was taken more than 10 days in this study. In 11.65% of participants, there was further episodes of diarrhea in our study. Side-effects, such as nausea and vomiting, following ingestion of zinc for the treatment of various medical problems, have been reported in adults and adolescents.[9]

Nasrin D et al, in their study on 320 children (n=320) aged less than five years, observed that 90.1% of 303 caretakers perceived that the tablets were equally or even more acceptable to their children compared to other formulations.[12] Statistically 98% of the children received the standard dose of one tablet per day, and 55.8%

completed the full 10-day course of zinc treatment in their study. Adherence rates did not vary by age or gender of the child.[12] In a cluster-randomized controlled trial in 2015 in eight districts of Ethiopia, it was observed that bundling zinc with ORS using a pouch with instructional messages increases adherence to the treatment. 'HC level bundling' is more CE than the 'central bundling' approach.[4] In this study, majority (45%) discontinued as diarrhoea stopped. In 37.5% of subjects, the reason for discontinuation was ignorance. Lamberti LM et al, in their study also observed that 69.5% of subjects discontinued treatment as the child recovered while in 27.1% of subjects, the child took another treatment.[11] In 12.5%, the reason for discontinuation was URI. There was no statistically significant difference between the groups classified based on further episodes of diarrhea with respect to compliance to zinc therapy and the number of days zinc was taken. The Ministry of Health and Family Welfare in India has launched the Intensified Diarrhea Control Fortnight (IDCF) in order to intensify efforts to reduce child deaths due to diarrhoea. During the fortnight, intensified community awareness campaigns on hygiene and promotion of ORS and Zinc therapy will be conducted at state, district and village levels. The compliance to complete 14-day zinc therapy was 62.14% in our study. The mean number of days zinc was taken was 11.28±3.81 days. In 11.65% of participants, there was further episodes of diarrhea. It can be concluded from study that zinc treatment is a simple, inexpensive, and critical tool for treating diarrheal episodes among children.

This study is limited by the reliance on caregiver reports to gauge provider instructions on zinc treatment dose and duration. The generalizability of our study findings is limited, as the study has been conducted in a single center. The lack of statistical significance of many of the differences between the study groups may be attributed to the smaller sample size. The role of potential confounding key variables could not be assessed due to a smaller sample size of the study. There is a need for large-scale multicentric studies, to enhance the quality of available evidence on the Indian population.

CONCLUSION

The compliance to complete 14-day zinc therapy was 62.14% in this study. Our results indicate moderate–to–good adherence to zinc treatment for diarrhea among caregivers in India. Programs aiming to scale–up zinc treatment for childhood diarrhea should train providers to successfully communicate dosing instructions to caregivers. These findings indicate that the syrup formulation is acceptable, but further efforts are required to enhance adherence. Our findings also highlight the importance of guiding in ensuring adherence to zinc duration while also addressing the tendency of caregivers to terminate treatment once a child appears to have recovered from an acute diarrheal episode.

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