



Effect of Zinc on Acute Diarrhea in Normal and Malnourished Children

Authors

Sharik R Navrungabade¹, Vaishali R Ghane²

^{1,2}Department of Paediatrics, ESIPGIMSR and ESIC Model Hospital, Andheri Mumbai.400 093

Corresponding Author

Dr Vaishali R. Ghane

Address: Bldg 2A- 1304, New MHADA Towers, Near Union Bank, Powai, Mumbai.400 072

Email: drvaishali_ghane@yahoo.co.in, Phone No: 9820442326

Abstract

Diarrhea constitutes a leading cause of morbidity and mortality among children less than five years of age in developing countries. Diarrheal diseases cause more than 3 million deaths each year and contribute substantially to malnutrition in surviving children. Studies have sufficiently described the beneficial effect of zinc in all types of diarrhea. Zinc helps by reducing the duration of diarrhea, especially in malnourished children. This study was designed to compare the severity of diarrhea in children receiving zinc plus ORS and other with ORS alone in normal and malnourished children.

The study included 100 patients, 50 belonging to each study and control group. In normally nourished patients partial recovery (2.69 ± 1.08 vs 3.94 ± 1.21 ; $P=8.91E-05$) and complete recovery (4.23 ± 1.66 vs 5.83 ± 1.76 ; $P=0.00021$) occurred earlier in study group. In children with malnutrition the mean duration in days for partial recovery (2.57 ± 1.09 vs 4.71 ± 1.27 ; $P=1.23E-03$) and complete recovery (4.00 ± 1.66 vs 6.57 ± 1.16 ; $P=0.00006572$) was less in study group. By Mann-Whitney test, the P value for partial and complete recovery is statistically significant. Among nutritionally normal patients the mean duration in hours (days) was (90.48 ± 52.8 { 3.77 ± 2.20 } vs 126.96 ± 50.64 { 5.29 ± 2.11 }; $P=0.00129$) less in study group. In malnourished patients the mean duration in hours (days) was (80.64 ± 46.8 { 3.36 ± 1.95 } vs 160.96 ± 69.04 { 6.89 ± 2.46 }; $P=0.000686$) less in study group and statistically significant by Mann-Whitney test.

To conclude we found that zinc causes early normalization of stool consistency and early recovery in both normal and malnourished children. It decreases total duration of hospital stay.

Keywords: acute diarrhea, partial recovery, complete recovery, hospital duration.

Introduction

Diarrhea constitutes a leading cause of morbidity and mortality among children less than five years of age in developing countries. It causes more than 3 million deaths of children in developing countries each year and contribute substantially to malnutrition in surviving children. ^(1,2)

Diarrhea is responsible for significant percentage of malnutrition and malnutrition related morbidity. Children who suffer from diarrhea are malnourished and have depleted micronutrient stores. Use of World Health Organization (WHO) ORS for treatment of acute diarrhea has become widespread since its introduction thirty years

back. WHO ORS corrects the dehydration and metabolic acidosis resulting from fluid and bicarbonate losses and reduces diarrhea related mortality. However, ORS alone does not decrease the duration of diarrhea or its consequences such as malnutrition^(1,2,3).

Studies have sufficiently described the beneficial effect of zinc in all types of diarrhea. Zinc helps by reducing the duration of diarrhea in malnourished children. Zinc causes early normalisation of stool consistency, early recovery, reduces total duration of hospital stay and the subsequent diarrhea related morbidity.^(1,2,3)

This study was designed to study effect of zinc on the severity of diarrhea in children at our institute and to identify any correlation with the nutritional status.

Material and Methods

This hospital based prospective study was conducted in paediatric department of a reference hospital over a period of 18 months. The study was conducted after approval from the institutional Ethics Committee. A written informed consent was obtained from the parents. Hundred children with acute diarrhea were enrolled with 50 each to study and control group. The alternate patients were randomized to study and control group. Patients of aged 6–59 months admitted with more than four episodes of loose stools in 24 hours were eligible for participation. Patients with presence of blood & mucous in stool, acutely ill, severely dehydrated were excluded from the study. The study group received ORS plus zinc and control group to received ORS alone. For study purpose an acute diarrhea was defined as acute onset of four or more loose, liquid stools per day of less than fourteen day duration. The change in stool consistency to semisolid was considered partial recovery. Complete recovery was defined as the change in stool to firm consistency and no loose stools for next 24 hours. Acute malnutrition was as per WHO's classification based on anthropometry parameters weight for height.

Patients demographic details, history and examination findings on admission were noted. Data included name, age, sex, registration number, h/o diarrhea duration, frequency of stool, character of stool (watery, mucoid or blood stained), fever, vomiting. Stool consistency (watery, semisolid, or firm) and its frequency (in 24 h) were checked and recorded. Nutritional assessment was done based on anthropometric data. Weight was measured by a digital weighting scale and infantometer was used to measure length of children below 24 months of age. Baseline investigations included hemogram and stool routine microscopy. The primary outcome was assessment of severity by observing normalisation of the stool consistency and the secondary outcome was duration of hospitalization.

The groups were compared using the chi-square test (or the Fisher exact test, if required) for the parametric variables. Statistical significance was based on two-sided design-based tests, Mann-Whitney test was applied with 0.05 level of significance and T- is replaced by Z-value. The statistical analysis was performed using SPSS version 16 for Windows.

Results

In this study total 100 patients were included and 50 patients each were allotted to study and a control group. As per age maximum children belonged to age group of 6 to 12 months (31{62%}vs 28{56%}) followed by 13 to 24 months(12{24%}vs 14{28%}). (Table 1)

The mean age for the patients in study and control group was 16.53 ± 11.39 and 16.31 ± 11.38 months respectively. Twenty eight (52.8%) male belonged to study group 25 (47.2%) to control group while 22 (46.8%) and 25(53.2%) females belonged to study and control group respectively. The mean weight (kgs) (8.65 ± 2.20 vs 8.57 ± 2.42), mean height (cms) (77.43 ± 9.32 vs 76.67 ± 11.09), mean weight for height percentage (86.14 ± 11.09 vs 87.90 ± 10.55) was comparable in study and control group. Ninety four (94%) patients stool

routine microscopy was normal and 2 (2%) patients of study group and 4 (4%) of control group had occasional pus cells but were culture negative. The baseline demographic data was comparable in both groups. (Table 1,2)

In normally nourished children the mean duration in days for partial recovery (2.69 ± 1.08 vs 3.94 ± 1.21 ; P value = $8.91E-05$) and complete recovery (4.23 ± 1.66 vs 5.83 ± 1.76 ; P value= 0.00021) was less in zinc supplemented group and was statistically significant. In children with acute malnutrition, the mean duration in days for partial recovery (2.57 ± 1.09 vs 4.71 ± 1.27 ; P= $1.23E-03$) and complete recovery (4.00 ± 1.66 vs 6.57 ± 1.16 ; P= 0.00006572) was less in zinc supplemented group and was statistically significant. (Table 3)

In nutritionally normal patients the duration of hospital stay in days/hours was (90.48 ± 52.8 hours { 3.77 ± 2.20 days} vs 126.96 ± 50.64 hours { 5.29 ± 2.11 days} p= 0.00129) less in zinc supplemented group. The mean duration of hospital stay in hours (days) among the malnourished patient, (80.64 ± 46.8 hrs { 3.36 ± 1.95 days} vs 160.96 ± 69.04 hrs { 6.89 ± 2.46 days P= 0.000686) was less in zinc supplemented group. By Mann-Whitney test the P value was statistically significant. Mann whitney test was applied where normality data failed and the P value was replace by Z value. (Table 4)

Tables of Effect of zinc on acute diarrhea in normal and malnourished children

Table 1 Age wise distribution of cases

Sr No.	Age group(months)	Study group (n=50)	Control group (n= 50)
1	6-12	31(62%)	28(56%)
2	13-24	12(24%)	14(28%)
3	25-36	4(8%)	5(10%)
4	36-48	1(2%)	3(6%)
5	49-56	2(4%)	0(0%)

Table: 2 Distribution of cases as per clinical characteristics

Parameter		Study n=50	Control N=50	P value
Age(months)		16.53	16.31	0.731
Gender	Male	28(52.8%)	25(47.2%)	0.689
	Female	22(46.87%)	25(53.2%)	0.689
Weight(Kgs)		8.65	8.57	0.759
Height(cms)		77.43	76.67	0.523
Weight/Height %		86.14	87.9	0.408
UMAC		13.36	13.25	0.685
Malnutrition	MAM	15(30%)	15(30%)	1.000
	Normal	35(70%)	35(70%)	1.000
Loose motions	Since days	2	3	0.505
	Frequency/day	8	9	0.366

Table 3: Clinical response in study and control group

No of days		Study	Control	P value	Significance
Partial recovery	Normal	3	4	$8.91E-05$	significant
	PEM	3	4	$1.23E-03$	significant
Complete recovery	Normal	4	6	0.00021	significant
	PEM	4	7	0.0000	significant

Table: 4 Average duration of hospital stay

Duration in days(hours)	Study	Control	P value
Normal	4(96)	5(120)	0.000
PEM	3(72)	6(144)	0.001

Discussion

The study evaluated the effectiveness of zinc as an adjunct to ORS in children of 6 months to 59 months with acute diarrhea admitted in our institute. The effectiveness of zinc was assessed by severity of the diarrhea in terms of change in stool consistency ie partial recovery and complete recovery. Duration of hospitalization was analysed as a secondary outcome. This study results confirmed that the addition of zinc supplements to routine ORS is associated with more favorable clinical course especially in malnourished children. The assessment of stool consistency confirmed earlier improvement in the zinc supplemented group. We excluded patients with probable bacterial etiology and included the ones who had features of viral diarrhea. Diagnostic microbiology study has been performed in only a few clinical trials so far.

In this study the baseline characteristics of the patients were similar to the studies conducted by Lukacik et al¹, Lazzerini², Muna et al³, Haider⁴, Sajid A⁵. Partial recovery in both normal and malnourished children occurred one day earlier in study group. Complete recovery was seen 2 days earlier in normal patients and 3 days earlier in malnourished children receiving zinc with ORS. (Table 3) Sangita Trivedi⁶ Mohammed Mohammad Karamyyar et. al.⁷ Bhatnagar S Bahl R et al⁸, Sunil Sazawal et al⁹, Lazzerini² reported clinically important reductions in the duration and severity of diarrhea following zinc supplementation in infants and young children.

The overall average duration of hospital stay was less in study group as compared to the control group. Studies by Sajid A⁵, Sangita Trivedi⁶ Mohammed Mohammad Karamyyar et. al.⁷, S K Roy¹⁰, Zulfiqar A¹¹ are from developing countries, based on the clinical hypothesis that malnourished children are zinc deficient and hence they show better clinical response to zinc supplementation. The results demonstrated by this study correlate with the above studies. The 70 % children enrolled were nutritionally normal while 30 % had malnutrition. Unlike other studies, both the

normal and malnourished children showed benefits of zinc supplementation. The reason for normally nourished children to show beneficial effect could be that even though anthropometrically normal they might be having subtle or borderline zinc deficiency. The duration of hospitalisation was also less in zinc supplemented group including both normal and malnourished children. S K Roy¹⁰, Al-Sonboli N¹², Dutta P¹³, had documented shortened duration, severity, early recovery in the cases of acute diarrhea and associated malnutrition. Zulfiqar A et¹¹ Al had reported beneficial effect of zinc in reducing the duration and severity of acute and persistent diarrhea. Our results of this study are correlating with the above studies.

The important limitation of our study was lack of baseline serum zinc level estimation. But our country being underdeveloped country with high incidence of malnutrition is considered high risk for zinc deficiency. It could be presumed that our patients might have had zinc deficiency: this might explain the considerable response to zinc supplements among our patients. To the contrary P Boranet al¹⁴ has documented zinc deficient levels and increments in zinc levels and yet not a significant response in reducing diarrheal duration, severity and morbidity in cases of acute diarrhea. Similarly Patel AB¹⁵ reported that the most important predictor for duration of diarrhea in children was the severity of the disease at enrolment, and not the zinc supplementation.

The overall beneficial effect of zinc supplement on morbidity and hospital duration has been analysed in economic perspective by Germana V. Gregorio¹⁶. The mean duration of diarrhea was 17 hours shorter and thereby mean total cost of treatment was 5% cheaper in zinc than ORS group. The present study has demonstrated the beneficial effect of zinc supplementation in reducing the severity and duration of acute diarrhea in normal as well as malnourished children of 6 months to 59 months of age. The zinc supplement is a cost effective and simple

intervention which can be practiced even in resource limited conditions.

Conclusion

Oral zinc supplementation in children with acute diarrhea, causes early normalization of stool consistency, early recovery and it thereby decreases total duration of hospital stay. Hence, zinc supplementation is effective, simple, acceptable and affordable intervention in management of acute diarrhea in children less than five years of age belonging to developing countries irrespective of their nutritional status.

Acknowledgements

The authors thank Dr. Mrs. Meenakshi Mathur, Dean ESIPGIMSR and ESIC Model Hospital Andheri, Mumbai for granting permission to publish this manuscript.

Funding: Nil

Conflict of interest: Nil

Ethical approval: Yes

Sources of support: Nil

References

1. Lukacik M, Thomas RL, Aranda JV. A meta-analysis of the effects of oral zinc in the treatment of acute and persistent diarrhea. *Pediatrics*. 2008; 121(2):326-336.
2. Lazzerini Marzia, Ronfani Luca. Oral zinc for treating diarrhea in children. *Cochrane Database of Systematic Reviews*. Sao Paulo Med J. 2011;129(2):118-9.
3. Muna A M Elnemr and Ahmed K Abdullah. Effect of Zinc Supplementation on Morbidity due to Acute Diarrhea in Infants and Children in Sanaa, Yemen :Arandomized controlled double blind clinical trial ; Sultan Qaboos Univ Med J. 2007 December; 7(3): 219–225.
4. Haider BA, Bhutta ZA. The effect of therapeutic zinc supplementation among young children with selected infections: a review of the evidence. *Food Nutr Bull*. 2009;30:S41-59. PubMed PMID: 19472601.
5. Sajid A, Sajid S, Ahmad M. Therapeutic role of zinc; Evaluation of in patients with diarrheal illnesses. *Professional Med J Sep* 2010;17(3):472-478.
6. Sangita S Trivedia, Rajesh K Chudasamab, Nehal Patel. Effect of Zinc Supplementation in Children with Acute Diarrhea: Randomized Double Blind Controlled trial: *Gastroenterology Research • 2009;2(3)168-174*.
7. Mohammad Karamyyar, Shahsanam Gheibim .Therapeutic Effects of Oral Zinc Supplementation on Acute Watery Diarrhea with Moderate Dehydration: A Double-Blind Randomized Clinical Trial:*Iran J Med Sci June 2013; Vol 38 No 2;93-99*.
8. Bhatnagar S, Bahl R, Sharma PK, Kumar GT, Saxena SK, Bhan MKJ *Pediatr Zinc with oral rehydration therapy reduces stool output and duration of diarrhea in hospitalized children: a randomized controlled trial Gastroenterol Nutr*. 2004 Jan;38(1):34- 40.
9. Sazawal, Sunil; Black, Robert E.; Bhan, Maharaj K.; Bhandari, Nita; Sinha, Anju; Jalla, Sanju. Zinc Supplementation in Young Children with Acute Diarrhea in India. *N Engl J Med*, Volume 333(13).Sep 28, 1995.839-844.
10. S K Roy, A M Tomkins, S M Akramuz-zaman, R H Behrens, R Haider, D Mahalanabis, G Fuchs. Randomised controlled trial of zinc supplementation in malnourished Bangladeshi children with acute diarrhea: *Archives of Disease in Childhood*.1997;77:196–200.
11. The Zinc Investigators' Collaborative Group (Zulfiqar A Bhutta, Sheila M Bird, Robert E Black, Kenneth H Brown, Julie Meeks Gardner, Adi Hidayat, et al Therapeutic effects of oral zinc in acute and persistent diarrhea in children in

- developing countries: pooled analysis of randomized controlled trials *Am J Clin Nutr* 2000;72:1516–22.
12. Al-Sonboli N, Gurgel RQ, Shenkin A, Hart CA, Cuevas LE. Zinc supplementation in Brazilian children with acute diarrhea. *Ann Trop Paediatr* 2003;23:3-8.
 13. Dutta P, Mitra U, Datta A, et al. Impact of zinc supplementation in malnourished children with acute watery diarrhea. *J Trop Pediatr* 2000; 46:259-63.
 14. P Boran, G Tokuc, E Vagas, S Oktem, and M K Gokduman: Impact of zinc supplementation in children with acute diarrhea in Turkey. *Arch Dis Child*. 2006 April; 91(4): 296–299.
 15. Patel AB, Dhande LA, Rawat MS. Therapeutic evaluation of zinc and copper supplementation in acute diarrhea in children: double blind randomized trial. *Indian Pediatr*. 2005 May;42(5):433-42.
 16. Germana V. Gregorio. Zinc supplementation reduced cost and duration of acute diarrhea in children. *Journal of Clinical Epidemiology* .Vol. 60 issue 6, pages 560-566, june 2007.