



COMPARATIVE STUDY OF ZINC IN DIFFERENT DOSAGE AND DURATION IN MANAGEMENT OF ACUTE DIARRHOEA IN CHILDREN

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ABSTRACT **Aims:** To study the effect of zinc therapy in different dosage and duration on stool frequency, total duration of diarrhoea and recurrence of acute diarrhoea.

Settings and Design: This study is Prospective hospital based study done in the Department of Pediatrics, JLN medical college and hospital, Ajmer from January 2015 to September 2015 (9 months) after ethical committee permission.

Methods and Material: Patients of acute diarrhoea admitted in children ward of age group between 6 months to 5 years were included in the study. Patients with Chronic diarrhoea, Persistent diarrhoea, Dysentery and Diarrhoea with any associated co-morbidity like fever and respiratory distress were excluded from study.

All cases enrolled in study were divided in five groups randomly from group A to E and all groups received low Osmolarity ORS. Group A have been given zinc 20 mg per day for 14 days, Group B zinc 20 mg per day for 10 days, Group C 10 mg for 14 days, Group D 10 mg per day for 10 days and Group E without zinc.

Statistical analysis:- Mean, Standard deviation, F-test, Z-test and P-value were used

Results: A 400 cases total were enrolled and during follow up 23 cases dropped out. Remaining 377 cases were taken among which 76(20.16%) in group A, 78(20.69%) in group B, 72(19.10%) in group C, 74(19.63%) in group D, 77(20.42%) in group E. There is no significant difference in total stool frequency among various groups. P-value is 0.200 (more than 0.05 is not significant).

F-ratio is 1.504 (less than 2.37 is not significant). There is no significant difference in total duration of diarrhea among various groups. F-value is 0.52 (less than 2.37 is not significant). P-value is 0.725 (more than 0.05 is not significant). There is significant difference in the reoccurrence of diarrhea among various groups. F-ratio is 3.39 (more than 2.37 is significant). P-value is 0.00 (less than 0.05 is significant).

Conclusions: The study revealed no statistical difference in stool frequency and duration of diarrhoea in zinc v/s non zinc group. Though there was a short follow up of 3 months. This study clearly indicates recurrence of diarrheal episode are less those who received Zinc therapy.

KEYWORDS : Acute Diarrhoea, Low Osmolarity ORS, Zinc

Introduction:

Acute diarrhoea is a leading cause of childhood death despite undeniable success of ORT. Worldwide, diarrhoeal diseases are the leading cause of pediatric morbidity and mortality, with 1.5 billion episodes and 1.5-2.5 million deaths estimated annually among children below 5 year of age.^{1,2} In Developing countries-infection, malnutrition and illiteracy worsen the scenario. One out of every five children who die of diarrhea worldwide is an Indian. Zinc deficiency common in developing countries because of overall food intake as well as the consumption of animal food is low.^{3,4} High stool frequency and duration of >14 days contributes to greater severity and risk of death.^{5,6} A significant reduction in the incidence of such severe episodes would justify adoption of measures to prevent zinc deficiency in susceptible population. Diarrhoea is consistently found in children with severe zinc deficiency^{7,8} as well as in animals with zinc depletion.⁹ Zinc deficiency leads to diarrhea, impairment of immune function^{10,11} and growth retardation (stunting).¹² ORT saves children's life but does not seem to have any effect on the length of time the children suffer from diarrhea. WHO, UNICEF in collaboration with USAID recommends zinc supplementation along with low osmolarity ORS in acute diarrhea which reduces duration and severity of episode and zinc supplementation given for 10-14 days lowers the incidence of diarrhea in next 2-3 months.¹³ WHO/UNICEF recommends zinc supplementation in acute diarrhoea at a dose of 10 mg/day for 10-14 days below 6 months and 20 mg/day for 10-14 days from 6 months to 5 years of age. The present study was done to evaluate the effect of zinc in different doses and duration on severity of acute diarrhoea in term of frequency, duration and recurrence.

Subjects and Methods:

This study is Prospective hospital based study done in the Department of Paediatrics, JLN medical college and hospital, Ajmer from January 2015 to September 2015 after ethical committee permission. A total of 400 cases were enrolled in the study and during follow up 23 cases were dropped so remaining 377 were taken in the study.

Patients of acute diarrhea admitted in children ward of age group between 6 months to 5 years were included in the study. Patients with Chronic diarrhea, Persistent diarrhea, Dysentery and Diarrhea with any associated co-morbidity like fever and respiratory distress were excluded from study. Patient who received ORS and zinc but who could not be followed up and those who not completed the zinc therapy as per dose and duration of specified group were included in drop out cases.

All patients have undergone detailed history and clinical examination to assess any degree of dehydration and associated co-morbidity. All cases enrolled in study were divided in five groups randomly from group A to E and all groups received low Osmolarity ORS. Group A have been given zinc 20 mg per day for 14 days, Group B zinc 20 mg per day for 10 days, Group C 10 mg for 14 days, Group D 10 mg per day for 10 days and Group E without zinc. Zinc supplementation has been given as oral zinc sulphate tablets as per group protocol with low Osmolarity ORS. During hospitalization, total no. of diarrheal episodes in 24 hrs and total duration of diarrhea in hrs from starting of zinc therapy to stopping of diarrheal episodes were recorded in printed proforma for each patient for every group.

We have taken complete address and contact number of parents of all five groups for purpose of follow up. After discharge we followed them telephonically for 3 months on every 15 days for recurrence of diarrhoeal episodes.

The statistical techniques used in the analysis of data are mean, standard deviation, F-test (ANOVA), Z-test and P-value.

Results:

A total of 400 cases were enrolled and during follow up 23 cases dropped out. Remaining 377 cases were taken among which 76(20.16%) in group A, 78(20.69%) in group B, 72(19.10%) in group C, 74(19.63%) in group D and 77(20.42%) in group E.

Out of 377 cases, 119 (31.56%) were from age group 6-12 months, 139(36.87%) were from age group 1-2 years, 49(12.99%) were from age group 2-3 years, 43(11.40%) were from age group 3-4 years and 27(7.16%) were from the age group of 4-5 years.

In the study male children were 210(55.70%) and female children were 167(44.30%).

Mean stool frequency in group A was 30.97, in group B 29.68, in group C 32.11, in group D 31.93 and in group E 33.83. P-value for stool frequency was 0.2 and F-ratio was 1.504 which was statistically insignificant to show effect of zinc therapy in different doses and duration on stool frequency.

Mean duration of diarrhea (in hours) in group A was 82.19, in group B 86.79, in group C 84.89, in group D 87.54 and in group E 87.03. P-value for diarrhea duration was 0.725 and F-ratio was 0.52 which was statistically insignificant to show effect of zinc therapy in different doses and duration on duration of diarrhea. Total duration of diarrhea was almost same in those who received zinc therapy in different doses and duration and those who not received zinc.

Recurrence of diarrhea noted in group A was 1.31%, in group B 2.56%, in group C 2.63%, in group D 4.05% and in group E 11.68%. P-value for recurrence was 0.00 (less than 0.05 which is significant) and F-ratio was 3.39 so there was statistically significant difference in recurrence of diarrhea between zinc and non-zinc group.

Though there was a short follow up of 3 months, but this study clearly indicates the significant difference in the recurrence between zinc and non-zinc groups. Those children who received zinc had little recurrence of diarrheal episodes as compared to those who did not received zinc in acute stage of diarrhea. Giving zinc in episode of acute diarrhea failed to help in current episode of diarrhea but certainly prevent recurrent diarrheal episode.

However our study was a small cohort study so large multicentre studies are required to evaluate our observations.

Discussion:

Effect of zinc therapy on total stool frequency- In our study there was no effect of different doses and duration of zinc therapy on total stool frequency. (P-value 0.2)

Archana Patel et al (2010) found that zinc supplementation reduce the mean duration of diarrhea by 19.7% but no effect on stool frequency and output and increases risk of vomiting¹⁴.

Wadhwa N et al (2011) found that median total stool output, diarrheal episode and duration of diarrhea was almost same in zinc and non-zinc group¹⁵.

Bahl R et al (2002) found that total number of stool was lower in the zinc ORS- group with the control group but there was no significant effect on diarrheal duration¹⁶.

Sazawal S et al (1995) found that in the zinc supplementation group there was a decrease of 39 percent in the mean number of watery stool per day¹⁷.

Effect of zinc therapy on total duration of diarrhea:

In our study there was no effect of different doses and duration of zinc therapy on total duration of diarrhea (P-value 0.725). Total duration of diarrhea was almost same in different group of patients in which we have given zinc therapy in different doses and duration and in which zinc therapy was not given.

Bahl R et al (2002) found that total number of stools was lower in the zinc-ORS group compared with the control group but there was no significant effect on diarrheal duration¹⁶.

Wadhwa N et al (2011) also found no difference induration of diarrhea in zinc- ORS group and ORS group¹⁵.

Haider BA et al (2009) provides evidence of reduction in the duration of acute diarrhea by 0.5 day (P-value 0.002) in children under 5 years of age. However zinc supplementation is found to have no beneficial impact in infants under 6 months of age¹⁸.

Bahl R et al and Wadhwa N et al supports our results while Haider BA et al have contrary results, this may be due to small sample size in our study.

Effect of zinc therapy on recurrence of diarrhea :

In our study we found that there was a significant difference in recurrence of diarrhea between zinc and non zinc group irrespective of doses and duration of zinc therapy (P-value <0.05). Recurrence rate was high in patients of non zinc group up to 3 months.

Adeniyi OS et al (2014) found that supplementation of zinc with ORS reduced the duration and severity of diarrheal episodes for up to 3 months¹⁹.

Gupta DN et al(2007) found that incidence of diarrhea was significantly less during the supplementation period (P- value<0.001) in zinc group²⁰.

Bhandari N et al (2002) zinc or placebo doses were administered on 88.8% and 91.2% respectively, of study days during the 4 months of follow up and found that zinc supplementation substantially reduce the incidence of severe and prolong diarrhea²¹.

All above studies shows same results as we found in our study that zinc reduces recurrence of diarrhea.

Conclusion :

This study show that the recurrence of diarrheal episode are significantly less those who received Zinc therapy during diarrhea episode.

TABLE 1: DISTRIBUTION OF CASES AMONG DIFFERENT GROUPS

Age in month	Group					Total
	A	B	C	D	E	
6-12	23	21	24	26	25	119
13 – 24	31	33	23	30	22	139
25 – 36	8	13	6	10	12	49
37-48	6	5	13	5	14	43
49-60	8	6	6	3	5	27
Total	76	78	72	74	77	377

Table-II Total stool frequency among various groups

Group	N	Mean	Standard deviation	f-ratio	p-value
A	76	30.97	14.42	1.504	0.200
B	78	29.68	9.11		
C	72	32.11	13.04		
D	74	31.93	8.17		
E	77	33.83	8.78		

Table-III Total duration of diarrhoea among various groups

Total Duration in Hours					
Group	N	Mean	Std. Deviation	F - Ratio	P- Value
A	77	82.19	34.57	0.52	0.725
B	78	86.79	28.20		
C	72	84.89	24.57		
D	74	87.54	19.27		
E	76	87.03	24.18		

Table- IV Recurrence of diarrhoea among various groups

Recurrence							
Group	N	Recurrence (no)	Recurrence (%)	Mean	Std. Deviation	F-Ratio	P-Value
A	76	1	1.31	1.01	0.20	3.39	0.00
B	78	2	2.56	1.03	0.16		
C	72	2	2.63	1.03	0.26		
D	74	3	4.05	1.04	0.25		
E	77	9	11.68	1.12	0.43		

References:

1. Kosek, M; Bern, C; Guerrant, RL. The global burden of diarrhoeal disease, as estimated

- from studies published between 1992 and 2000. *Bull. World Health Organ* 2003, 81, 197–204.
2. Black, RE; Morris, SS; Bryce, J. Where and why are 10 million children dying every year? *Lancet* 2003, 361, 2226–2234.
 3. Diarrhea claims nearly 1000 children in India every day: Report. [last cited on 2010 Feb 12]. Available from: <http://www.medindia.net/news/Diarrhea-Claims-Nearly-1000-Children-in-India-Every-Day-Report-26603-1.htm>.
 4. Castillo-Duran C, Vial P, Uauy R. Trace mineral balance during acute diarrhea in infants. *J Pediatr* 1988;113:452–7.Hj
 5. Fernades, G., Nair, M., Onoe, K., Tanaka, T., Floyd, R. and Good, R. A. 1979. Impairment of cell mediated immunity functions by dietary Zn deficiency in mice. *Proc. Natl. Acad. Sci. U. S. A.*, 76: 457–461. Hj
 6. Shankar AH, Prasad AS. Zinc and immune function: the biological basis of altered resistance to infection. *Am J Clin Nutr* 1998; 68(suppl):447S–63S.
 7. Moynahan, E.J. ACRODERMATITIS ENTEROPATHICA: A LETHAL INHERITED HUMAN ZINC-DEFICIENCY DISORDER *The Lancet*, Volume 304, Issue 7877, 399–400
 8. Kay RG, Tasman-Jones C Letter: Zinc deficiency and intravenous feeding *Lancet*. 1975 Sep 27;2(7935):605-6
 9. Tomkins, A., Behrens, R., & Roy, S., (1993). The role of zinc and vitamin A deficiency in diarrhoeal syndromes in developing countries. *Proceedings of the Nutrition Society*, 52(1), 131-142. Doi:10.1079/PNS19930045
 10. Beisel WR. Single nutrients and immunity. *Am J Clin Nutr*. 1982 Feb;35(2 Suppl):417-68
 11. Golden MHN, Golden BE. Zinc and delayed hypersensitivity responses. *Nutr Res* 1985;5:Suppl1:S-700
 12. Allen LH. Nutritional influences on linear growth: a general review. *Eur J Clin Nutr* 1994;48:Suppl 1:S75-S89
 13. WHO. Clinical management of acute diarrhoea. Geneva/New York: World Health Organization/UNICEF; 2004. (http://www.who.int/maternal_child_adolescent/documents/who_fch_cah_04_7/en/)
 14. Patel A, Mamtani M, Dibley MJ, Badhoniya N, Kulkarni H (2010) Therapeutic Value of Zinc Supplementation in Acute and Persistent Diarrhea: A Systematic Review. *PLoS ONE* 5(4): e10386. <https://doi.org/10.1371/journal.pone.0010386>
 15. Wadhwa N, Natchu UC, Sommerfelt H, Strand TA, Kapoor V, Saini S, Kainth US, Bhatnagar S. ORS containing zinc does not reduce duration or stool volume of acute diarrhea in hospitalized children. *Journal of Pediatric Gastroenterology and Nutrition*. 2011;53(2):161–167. doi: 10.1097/MPG.0b013e318213ca55
 16. Bhandari N, Bahl R, Taneja S, Strand T, Mølbak K, Ulvik RJ, Sommerfelt H, Bhan MK. Substantial Reduction in Severe Diarrheal Morbidity by Daily Zinc Supplementation in Young North Indian Children. *Pediatrics* June 2002, VOLUME 109 /ISSUE 6
 17. Sazawal S, Black RE, Bhan MK, Bhandari N, Sinha A, Jalla S: Zinc supplementation in young children with acute diarrhea in India. *N Engl J Med* 333: 839–844, 1995
 18. Haider BA, Bhutta ZA (2009) The effect of therapeutic zinc supplementation among young children with selected infections: a review of the evidence. *Food Nutr Bull* 30: S41–59.
 19. Adeniyi O. S., Akomolafe RO, Ojabo CO, Eru EU, Olaleye SB. Effect of zinc treatment on intestinal motility in experimentally induced diarrhea in rats. *Niger. J. Physiol. Sci.* 29(June 2014)011–015
 20. Gupta DN, Rajendran K, Mondal SK, Ghosh S and Bhattacharya SK. Operational feasibility of implementing community-based zinc supplementation: impact on childhood diarrhoeal morbidity. *The Pediatric Infectious Diseases Journal* 2007; 26: 306-310.
 21. Bahl, R.; Bhandari, N.; Saksena, M.; Strand, T.; Kumar, G.T.; Bhan, M.K.; Sommerfelt, H. Efficacy of zinc-fortified oral rehydration solution in 6- to 35-month-old children with acute diarrhea. *J. Pediatr.* 2002, 141, 677–682, doi:10.1067/mpd.2002.128543.