EFFICACY AND EFFECTIVENESS OF ZINC THERAPY IN THE TREATMENT OF ACUTE DIARRHOEA AMONG CHILDRENRazin Nazarullah¹, Swapna K. Pillai², P. M. C. Nair³**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: BACKGROUND: Diarrhoea is one of the leading causes of morbidity and mortality affecting children in developing countries. We studied the efficacy of zinc therapy in reducing the duration of diarrhoea. **MATERIALS AND METHODS:** A double- blinded randomized control study was done in 100 children between age groups 1 month to 5 years having acute diarrhoea. These children were randomly divided into 2 groups. Group 1 received oral supplementation of 20mg zinc and ORS from day one of treatment while group 2 received only ORS therapy. Children who received zinc or antibiotics prior to the study were excluded. Clinical profile of children like age, gender, nutritional status and dehydration level was have been taken into consideration. The outcome of the study was assessed by comparing the mean number of watery stools of both the groups during the course of therapy. **RESULTS:** Out of 100 children based in the study 50 children in group 1 who received oral zinc supplementation showed a 36% reduction in duration of diarrhoea (6.22 days vs. 8.26 days). **CONCLUSION:** Zinc supplementation help reduce the duration of acute diarrhoea.

KEYWORDS: Zinc, Diarrhoea.

INTRODUCTION: Diarrhoeal disease is a major cause of childhood morbidity and mortality affecting millions of children worldwide.^(1,2) It is estimated that more than 3 million deaths in developing countries each year is caused by diarrhoeal disease and contribute substantially to malnutrition in surviving children.⁽²⁾

In accordance with the recommendations of WHO and UNICEF over the past 3 decades children of all ages including infants with acute diarrhoea of any etiology have been treated with standard oral rehydrating salt (ORS) solution.⁽³⁾ Due to proven efficacy, safety and low cost, standard ORS has been widely used. Along with continued feeding, ORS has helped to bring about a decline in the fatality rate of acute dehydrating diarrhoea in children in developing countries⁽³⁾. However with the use of ORS there is no reduction of stool volume, diarrhoeal duration and frequency of loose stools raising a practical problem of its acceptance and compliance.⁽⁴⁾

Studies have reported that daily loss of zinc in the intestinal fluid during acute diarrhoea is as high as 159 mic/kg/day compared to 47 mic/kg/day in control.⁽⁵⁾ A simple and sensitive measuring tool for zinc status is lacking, It can however be assumed that because of low bioavailability of zinc from cereal based diet⁽⁶⁾ subclinical zinc deficiency is common in developing countries. Few children with acute diarrhoea also have lowered immunity as manifested by the absence of a cell mediated response to common antigen applied to skin. Micronutrient deficiency is the most likely explanation for this phenomenon.⁽⁷⁾ Zinc is important for growth of intestinal mucosa and improves the transport of water and electrolytes⁽⁸⁾ across the intestinal mucosa. Zinc also is essential in growth, protein synthesis, epithelial repair and synthesis of RNA and DNA.⁽⁹⁾

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MATERIALS AND METHODS: 100 children between age groups 1 month to 5 years having acute diarrhoea form the study group out of which group2 will serve as control and group 1 will be supplemented with zinc. Children with persistent diarrhoea and dysentery, zinc supplementation prior to admission had been excluded.

OUTCOME MEASURES: The study was analysed on basis of outcome after day 7 of therapy, Mean number of watery stools per day, Mean duration of hospitalization.

STATISTICAL ANALYSIS:

1. Chi Square Test.
2. Student t Test.
3. Fisher Exact Test.

DATA ANALYSIS:

1. Characteristics of study population.
2. Disease Characteristics.
3. Analysis of outcome measures.

RESULTS: The baseline characteristics of the enrolled children with regard to age were comparable in both groups. Majority of the children enrolled in the study were between 6 months to 2 years. This finding is consistent with the hospital statistics.

Graph 1: Age distribution

CHARACTERISTICS OF THE STUDY POPULATION:

AGE IN MONTHS	GROUP 1	PERCENTAGE (%)	GROUP 2	PERCENTAGE (%)
01 - 12	16	32	12	24
13 - 24	12	24	16	32
25 - 36	11	22	11	22

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37 – 48	07	14	06	12
49 – 60	04	08	05	10
TOTAL	50		50	

TABLE 1: AGE DISTRIBUTION

$\chi^2 = 1.33$; d.f = 4; P Value = 0.8561 (Not Significant)

The baseline characteristics of the enrolled children, with regard to age were comparable in both groups. Majority of the children enrolled in the study were between 6 months to 2 years. This finding is consistent with the hospital statistics were majority of the children with acute diarrhoeal disease are between 6 months to 2 years of age.

Graph 2: Sex distribution

SEX	GROUP 1	PERCENTAGE (%)	GROUP 2	PERCENTAGE (%)
MALE	29	58	30	60
FEMALE	21	42	20	40

TABLE 2: SEX DISTRIBUTION

Fisher Exact Test P Value = 0.5 (Not Significant)

Children in both the groups had similar sex distribution and were comparable. There was a slight predominance of male children among the enrolled in the study. In group I 58% of the enrolled children was males and in group II 60 % of the enrolled children were males with a total average of 59%.

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Graph 3: Nutritional status

NUTRITIONAL STATUS	GROUP 1	PERCENTAGE (%)	GROUP 2	PERCENTAGE (%)
GRADE 1	15	30	13	26
GRADE 2	03	06	01	02
NORMAL	32	64	36	72
TOTAL	50		50	

TABLE 3: NUTRITIONAL STATUS

$\chi^2 = 1.378$; d.f = 2; P Value = 0.502 (Not Significant)

Nutritional status was assessed using the Indian Academy of Pediatrics classification based on specific weight. The status of nutrition was similar in both the groups and they were comparable. Majority of the children in our study had normal nutritional status (group I - 64 %, group II - 72%).

Graph 4: Duration of diarrhea on hospitalization

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DISEASE CHARACTERISTICS:

DURATION OF DIARRHOEA	GROUP 1	PERCENTAGE (%)	GROUP 2	PERCENTAGE (%)
< 24 Hrs.	10	20	11	22
24 – 48 Hrs.	12	24	19	38
48 – 72 Hrs.	22	44	18	36
> 72 Hrs.	6	12	2	4
TOTAL	50		50	

Table 4: Duration of diarrhoea on hospitalization

$X^2 = 4.0283$; d.f = 3; P Value = 0.2584 (Not Significant)

The baseline characteristics of the disease with regard to duration of diarrhoea were similar in both the groups and were comparable. The duration of diarrhoea was less than 3 days in majority of children. 88% of children in group I and 96% of children in group II have duration of diarrhoea less than 3 days.

Graph 5: Number of loose stools on hospitalization

NUMBER OF STOOLS	GROUP 1	PERCENTAGE (%)	GROUP 2	PERCENTAGE (%)
0 – 5	02	04	01	02
6 -10	09	18	08	16
11 – 15	29	58	32	64
16 – 20	10	20	09	18
TOTAL	50		50	

TABLE 5: TOTAL NUMBER OF LOOSE STOOLS ON HOSPITALIZATION

$X^2 = 0.5923$; d.f = 3; P Value = 0.8982 (Not Significant)

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The total numbers of loose stools in both the groups were comparable. Most of the children had 11–15 loose stools at the time of admission to hospitals. 64% of children in group 1 and 58% of children of group II had stool output in the frequency of 11-15.

Graph 6: Distribution according to hydration status

HYDRATION STATUS	GROUP 1	PERCENTAGE (%)	GROUP 2	PERCENTAGE (%)
NO	12	24	10	20
SEVERE	02	04	01	02
SOME	36	72	39	78
TOTAL	50		50	

TABLE 6: DISTRIBUTION ACCORDING TO HYDRATION STATUS

$X^2 = 0.6352$; d.f = 2; P Value = 0.7279 (Not Significant)

There was no significant difference in the hydration status of the children in both the groups. The hydration status in both the groups was comparable. Most of children admitted were with some dehydration. 72 % of children in group I and 78% of children of group II presented with signs suggestive of some dehydration.

Graph 7: Distribution according to watery stools on day 4 to 7

WATERY STOOLS	GROUP 1	PERCENTAGE (%)	GROUP 2	PERCENTAGE (%)
PRESENT	20	40	38	76
ABSENT	30	60	12	24
TOTAL	50		50	

TABLE 7: DISTRIBUTION ACCORDING TO WATERY STOOLS ON DAY 4 TO 7

Fisher Exact Test P Value = 0.00025 (Not Significant)

Statistical analysis on days 4–7 showed that there was moderate reduction the risk of continued diarrhoea as indicated in the absence of watery stools among children in group I. 76 % of children in group II still continued to have watery diarrhoea whereas only 40% of children in Group I continued to have watery diarrhoea. On comparison between the two groups it was observed that there was a 36% reduced risk of continued diarrhoea in Group I.

Graph 8: Distribution according to watery stools after day 7

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WATERY STOOLS	GROUP 1	PERCENTAGE (%)	GROUP 2	PERCENTAGE (%)
PRESENT	16	32	32	72
ABSENT	34	68	14	28
TOTAL	50		50	

TABLE 8: DISTRIBUTION ACCORDING TO WATERY STOOLS AFTER DAY 7

Fisher Exact Test P Value = 0.000059 (Not Significant)

Statistical analysis after 1 week showed that there was moderate reduction the risk of continued diarrhoea as indicated by the absence of watery stools among children in group I. 72% of children in group II still continued to have watery diarrhoea whereas only 32% of children in Group I continued to have watery diarrhoea. On comparison between the two groups it was observed that there was a 40% reduced risk of continued diarrhoea in Group I.

Graph 9: Distribution according to reduction in risk of continued diarrhea

NUTRITIONAL STATUS	N	GROUP 1	N	GROUP 2	T - TEST (P - VALUE)
NORMAL	32	6.5 ± 2.21	36	8.55 ± 2.13	0.00011
GRADE 1	15	5.71 ± 1.624	13	7.384 ± 2.328	0.018
GRADE 2	03	5.67 ± 2.516	01	9 ± 1.6	0.0072

TABLE 9: DISTRIBUTION ACCORDING TO NUTRITIONAL STATUS VS. MEAN DURATION OF DIARRHOEA

The nutritional status and mean duration of Diarrhoea was compared and it was observed that there was a significant reduction in the duration of diarrhoea in children with Grade II PEM and Grade I PEM than the children with normal nutritional status. There was a reduction of 30% in the

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mean duration of diarrhoea in children with Grade II PEM and Grade I PEM between Group II and Group I.

CONCLUSION: 20mg of zinc supplementation reduced the risk and duration of acute diarrhoea. Zinc supplementation was also associated with fast recovery and reduced hospitalization. There was reduction in duration of diarrhoea in children with grade 2 PEM.

DISCUSSION: The role of zinc in protein energy malnutrition and acrodermatitis enteropathica has been well established by numerous studies. This pilot study seeks to determine the role of zinc in acute diarrhoea and there supplementation on the outcome.

Our study documents the effectiveness of zinc supplementation as an adjunct to oral rehydration therapy. Zinc supplementation was associated with a clinical important and statistically significant reduction in the mean duration of diarrhoea in children with under nutrition and with some dehydration. It also resulted in significant reduction in frequency stools.

Among the children who received zinc, estimates of likelihood of recovery revealed a reduction of 36% in the risk of continued diarrhoea during day 3 to 7 and a reduction of 40% after day 7 which is significant. The zinc supplemented children had a significant reduction in the duration of diarrhoea (6.22 vs 8.26 days). In these studies the duration of diarrhoea was more reduced in malnourished children (46) and dehydrated children. In our study there was a significant reduction of mean duration of diarrhoea in children with grade 2 malnutrition (30%) and children with some and severe dehydration(23.4% and 18.1%).

The comparison of the effects of supplementation among subgroups indicate the dehydration and nutrition status or both can be used to select the children most likely to benefit from the treatment with zinc. The possible mechanisms for the effect of zinc supplementation in diarrhoea include improved absorption of water and electrolytes, regeneration of gut epithelium and the restoration of its function, increased level of enterocyte brush border enzymes and enhanced immunological mechanisms for the clearance of infection including increased cellular immunity and higher level of secretory antibodies. It is also possible that improved appetite and dietary intake resulted in shorter episode of diarrhoea as a result of the effects of staple foods on the stool consistency. Recent studies have also shown that enteral zinc supplementation helps in weight gain and growth of extreme low birth weight babies.⁽¹⁰⁾

In conclusion oral zinc supplementation resulted in clinically important reduction in duration and severity of diarrhoea, hence the use of zinc as adjunctive therapy has the potential to improve the management of diarrhoea and increase survival in children. It helps reduction of morbidity and mortality due to diarrhoeal disease in children in our country who are likely to be malnourished. With all the above mentioned advantages the simple cost effective method of oral zinc supplementation can be incorporated into diarrhoeal disease control program in developing countries.^(11,12)

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