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Original Research Article

Zinc Supplementation For Diarrhoea

A Study on Zinc Utilization in the Treatment of Acute Diarrhoea among The Paediatric In - Patients of JNIMS Hospital, Imphal – A Retrospective Study

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Abstract: Acute diarrhoeal disease is a public health problem. Treatment of this disease with ORS along with zinc supplementation is a big challenge. Zinc supplementation in the treatment of diarrhoea has shown to decrease the duration and severity of diarrhoeal episodes and hospitalization rates. The study examines the role of Zinc in the management of acute diarrhoea among paediatric in-patients in JNIMS Hospital, Imphal. Zinc is necessary for physiological processes including defence against infections. Zinc deficiency is responsible for 4% of global child morbidity and mortality[1]. Zinc supplements given for 10–14 days together with low-osmolarity oral rehydration solution (Lo-ORS) are recommended for the treatment of childhood diarrhoea. In children aged =6 months, daily zinc supplements reduces the duration of acute diarrhoea episodes by 12 hours and persistent diarrhoea by 17 hours. The present study was undertaken to study the effect of zinc supplementation in the treatment of acute paediatric diarrhoea. A retrospective observational study was conducted among paediatric patients in JNIMS paediatric ward for a period of 6 months from October 2020 to March 2021.A total of 160 case sheets were collected for the study.{92(57.5%) males and 68 (42.5%) females}. The data collected included demographics of the children, diagnosis and line of management. Descriptive statistics were used to analyse the observations. The group of patients receiving ORS with Zinc showed significant reduction in frequency of diarrhoeal episodes on the third day of treatment as compared to the group of patients given only ORS without Zinc ($p<0.001$). Administration of Zinc with ORS was found to reduce the mean duration of hospital stay.

Keywords: Zinc, Diarrhoea, ORS, Child Morbidity, Child Mortality

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1. INTRODUCTION

Zinc deficiency is a common component of undernutrition and is associated with stunting and diarrhoea, particularly in children < 5 years of age[1]. Diarrhoea is defined as increase in episodes of defecation more than three times per day and/or loosened stool consistency, and/or increased stool weight (>200 gm/day). The main cause of diarrhoea among children worldwide is rotavirus that is responsible for 40% of hospitalized cases. The primary symptoms of rotavirus diarrhoea are fever, vomiting and non bloody diarrhoea. It is estimated that diarrhoeal disease causes 1.5 - 2.5 million deaths per year. But the morbidity and mortality due to diarrhoea has reduced with the introduction of oral rehydration therapy through the WHO - ORS formulation. The introduction of oral rehydration therapy for the treatment of the dehydration and metabolic acidosis associated with acute diarrhoea has been claimed by many as one of the most important therapeutic advances of the past century[3].The physiologic basis for oral rehydration solution (ORS) was the demonstration that (1) absorptive and secretory processes in the small intestine are separate and distinct, (2) cyclic nucleotides induce chlorine (Cl)-induced fluid secretion without affecting glucose-stimulated sodium (Na) absorption, and (3) glucose enhances Na and fluid absorption without modifying fluid secretion[4]. Many modifications and improvements of the WHO-ORS formulation, like rice based or cereal based formulations have been found to be quite useful in the management of diarrhoea. Recently, Zinc (Zn) which is an essential micronutrient has also been used as an add on with the UNICEF modified ORS in the management of diarrhoea. This mode of therapy is implemented under the Rural Health Mission (RHM, Govt of India). This model of therapy substantially reduces the duration and severity of acute and chronic diarrhoea in children. Inclusion of Zinc in ORS has many advantages. Zinc inhibits chloride secretion and enhances sodium absorption. Therefore, nowadays Zinc is a much needed inexpensive item for prevention and treatment of diarrhoeal diseases. Diarrhoea remains the 2nd leading cause of death among children under 5 years in developing countries. Zinc for the treatment of diarrhoea has been recommended by WHO and UNICEF since 2004. But access to this essential treatment remains limited. Zinc is essential for maintaining the structure and form of protein molecules; it is in many cases fundamental to their function as enzymes or structural proteins. Diverse physiological processes including cell replication are impacted by zinc deficiency. Of particular relevance to public health, Zinc is necessary for immune defence systems, growth, intestinal function, and brain development. Zinc sulphate has also been found to have anti-oxidant property although exact mechanism is yet to be explored[5]. It is estimated that 35% of child deaths can be attributed to undernutrition which increases the risk and severity of infectious diseases such as diarrheal disease, pneumonia and malaria[6]. When given for 10 - 14 days during and following the diarrhoeal episode, Zinc has been shown to decrease the duration and severity of the diarrhoeal episode as well as decrease the incidence of diarrhoeal episode in the subsequent 2 - 3 months. Many investigators participating in the management of diarrhoeal diseases of children under 5 years included Zinc in addition to ORS in the management of acute diarrhoea and observed the effect on duration of diarrhoea as well as duration in hospitalization and mortality. The findings in this study also acknowledged the findings of the previous investigators. Zinc along with ORS reduced the hospital mortality by 23% and also decreased diarrhoea prevalence in both 24 hours and 2 weeks. Only a very small proportion of children in need have access to Zinc supplementation. Use of Zinc supplementation in the management of diarrhoea has accelerated progress towards the United Nations Milennium Development Goal and has drastically reduced child mortality by about two thirds as of 2015.[7] Zinc provides substantial benefit in terms of induction of cation absorption and/or inhibition of anion secretion along with reduction of stool output and disease duration. Zinc is inexpensive, easy to administer, safe and well tolerated[4]. Administration of Zinc + ORS in children (2 months to 4 years) has reduced episodes of acute diarrhoea[8]. Zinc supplementation has been used to combat zinc deficiency in young children, as an adjunct in treatment of common infectious diseases. Meta-analysis of trials of adjunctive zinc supplementation in children with diarrhoea has shown that the duration of the illness has been reduced by 24%[9]. According to WHO, children are to be given with 20 mg per day of zinc supplementation for 10– 14 days (10 mg per day for infants < 6months)[1]. The aim and objective of the present study is to examine the role of Zinc in the management of acute diarrhoea among paediatric inpatients taking Oral Rehydration Therapy. Oral rehydration therapy (ORT) programmes are being taken up nationwide as an essential component of National Rural Health Mission (NRHM).

2. MATERIALS AND METHODS

It was a retrospective observational study of the hospital Bed Head Tickets (BHTs) for a period of 6 months. BHTs of paediatric in-patients from October 2020 to March 2021 were collected for the purpose of the study. The study was conducted in accordance with the ethical standards given in 1964 (Declaration of Helsinki revised in 2013). The study protocol was submitted to the Head of the Hospital i.e., Medical Superintendent of JNIMS Hospital and due permission was given to study the Bed Head Tickets (BHTs) of paediatric patients via Approval no- Res-Project/Pharma/2016 obtained on 30/04/2020. The consent for examination of the case sheets for each of the paediatric patients was obtained from the Medical Record Officer (MRO), JNIMS Hospital. Data collected from the case sheets were name, age, sex, address, parents name of the children, co- administered drugs, number of hospital days. Since our study is a retrospective study of the case-sheets, we took the actual number of cases receiving the different modalities of treatment from among the in-patients.

2.1 Inclusion criteria

1. Children of either sex in age group of 1 month to 10 years admitted in JNIMS Paediatric ward.
2. Children receiving complete treatment for diarrhoea during stay in the hospital.

2.2 Exclusion criteria

1. Children who left against medical advice after starting treatment.
2. Children receiving treatment for other co-morbid conditions.

3. STATISTICAL ANALYSIS

The data obtained were analysed by using SPSS version 20. One way ANOVA descriptive statistical analysis was used for

comparison. The data were presented as mean ± standard deviation (SD). Probability value (P) of less than 0.05 was considered statistically significant.

4. RESULTS

Out of 180 case sheets collected, 160 case sheets were observed for the management of acute diarrhoea in children of 1 month to 10 years. The children were 92 (57.5%) males and 68 (42.5%) females (Table 1). The children in the age group of 1 to 3 years were 68 in number (42.5%) and children of 8 – 10 years were 2 in number (1.25%). Further, on examination, the utility of ORS with or without Zinc supplementation was observed. Frequency of patients receiving ORS with or without Zinc supplementation was observed. Frequency of patients receiving ORS with Zinc, ORS alone and Zinc alone were 109, 32 and 3 respectively (Table 2). The mean frequency of stool on the first day of admission for the group of children receiving ORS with Zinc was 6.04 ± 0.223, whereas the mean frequency of stool on the third day of treatment for the same group was 1.08 ± 0.324. The mean frequency of stool on the first day of admission for the group of children receiving ORS only was 5.90 ± 1.832, whereas the mean frequency of stool on the third day of treatment for the same group was 1.46 ± 0.509. So, the group of patients receiving ORS with Zinc showed significant reduction in frequency of diarrhoeal episodes on the third day of treatment as compared to the group of patients given only ORS without Zinc. Out of 109 patients given ORS with Zinc, 32 (20%) stayed for 3 days in the hospital (Table 3). Zinc supplementation in the management of acute diarrhoea was found to shorten the duration of hospital stay with decrease in frequency of stool in comparison to administration of ORS without Zinc. The mean duration of hospital stay for children receiving Zinc alone was 5.33. The mean duration of hospital stay for children receiving ORS with Zinc was 3.06 while the mean duration of hospital stay for the group of children receiving ORS only was 5.0 (Table4).

Table 1: Paediatric in-patient characteristics

Age group in months	Male (%)	Female (%)	Total (%)
Under 12	38 (23.75%)	24 (15%)	62 (38.75%)
13 - 36	**43 (26.87%)**	**25 (15.62%)**	**68 (42.5%)**
37- 72	5 (3.12%)	10 (6.25%)	15 (9.37%)
73 - 108	4 (2.5%)	9 (5.62%)	13 (8.12%)
109 and older	2 (1.25%)	0 (0.00%)	2 (1.25%)
Total	92 (57.5%)	68 (42.5%)	160 (100%)

N=160 (Total paediatric inpatients)

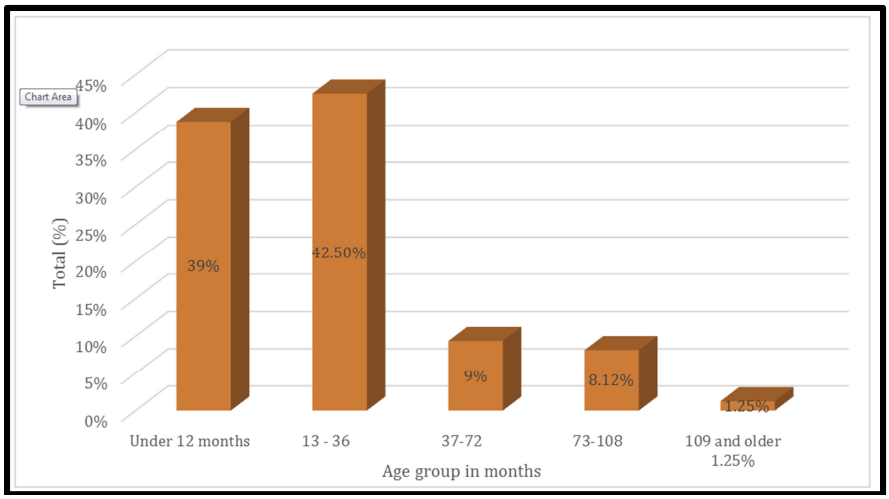

FIG: Paediatric in-patient characteristics

Table 2: Table showing frequency of stool on day 1, 2 and 3 of hospital stay in comparison between the group given ORS alone with the group given ORS along with Zinc in treatment

Groups of patients	Number of paediatric inpatients (%)	Mean frequency of stool on day 1, 2 and 3	P value
Day1:			
ORS alone	31(19.37%)	5.90 ± 1.832	0.770
ORS + Zinc	109(68.12%)	6.04 ± 2.333	
Total	140(87.5%)	6.01 ± 2.226	
Day2:			
ORS alone	27(16.87%)	2.59 ± 0.844	0.003
ORS + Zinc	99(61.87%)	1.93 ± 1.062	
Total	126(78.75%)	2.07 ± 1.052	
Day3:			
ORS alone	24(15.00%)	1.46 ± 0.509	0.000
ORS+ Zinc	64(40.00%)	1.08 ± 0.324	
Total	88(55.00%)	1.18 ± 0.416	

Given here, mean frequency of stool on day 1, 2, 3 with SD (standard deviation), and comparing means between the group I & II on day 1 of treatment, group I & II on Day 2 of treatment, group I & II on day 3 of treatment by using one way ANOVA descriptive analysis are found to be significant on day 2 and 3 of treatment with p=0.003 and 0.000, p<0.05(significant)

Group I: In - patients given ORS alone, Group II: In- patients given ORS with Zinc

Table 3: Table showing duration of hospital stays for groups of in - patients given ORS alone, ORS along with Zinc and Zinc alone respectively.

Duration of hospital stay in days	Groups of in-patients given none (A)	Groups of in-patients given ORS alone (B)	Group of in-patients given ORS with Zinc (C)	Group of in-patients given Zinc alone (D)	Total in-patients (%) (N)
1	3 (1.87%)	4 (2.5%)	12 (7.5%)	0 (0.00%)	19 (11.87%)
2	7 (4.37%)	4 (2.5%)	35 (21.87%)	0 (0.00%)	46 (28.75%)
3	3 (1.87%)	0 (0.00%)	32 (20.00%)	0 (0.00%)	35 (21.87%)
4	1 (0.62%)	2 (1.25%)	15 (9.37%)	1 (0.62%)	19 (11.87%)
5	2 (1.25%)	3 (1.87%)	9 (5.62%)	1 (0.62%)	15 (9.37%)
6	0 (0.00%)	12 (7.5%)	2 (1.25%)	0 (0.00%)	14 (8.75%)
7	0 (0.00%)	3 (1.87%)	3 (1.87%)	1 (0.62%)	7 (4.37%)
8	0 (0.00%)	4 (2.5%)	0 (0.00%)	0 (0.00%)	4 (2.5%)
17	0 (0.00%0	0 (0.00%)	1 (0.62%)	0 (0.00%)	1 (0.62%)
Total	**16 (10.00%)**	**32 (20.00%)**	**109 (68.12%)**	**3 (1.87%)**	**160 (100%)**

N=160
Group A: in-patients given none
Group B: in-patients given ORS alone
Group C: in-patients given ORS with Zinc
Group D: in-patients given Zinc alone

Table 4: Comparison of mean duration of hospital stay in days among the different groups of in-patients given ORS alone, ORS with Zinc, Zinc alone and none for treatment respectively.

Groups of in-patients	Mean duration of hospital stay	Total number of inpatients	P value
Group of patients given ORS alone	**5.00**	**32**	**0.000 (highly significant)**
Group of patients given ORS with Zinc	**3.06**	**109**	
Group of patients given Zinc alone	**5.33**	**3**	
Group of patients given none	**2.50**	**16**	

By using one way ANOVA descriptive statistical analysis, means of the different groups ie., group I, II, III and IV are compared between and within the groups and are found to be highly significant with p=0.000. p<0.05 (significant).

5. DISCUSSION

In our study population, children who received Zinc supplementation had shorter duration and lower incidence of diarrhoea. The reduction in the duration of diarrhoeal episodes is consistent with earlier studies[10,11].Possible mechanisms for the effect of Zinc treatment on the duration of diarrhoea include improved absorption of water and electrolytes by the intestine,[12] faster regeneration of gut epithelium[13], increased levels of enterocyte brush border enzymes[14], and enhanced immune response[15], leading to early clearance of diarrhoeal pathogens from the intestine[16]. Three studies in which Zinc was given for two weeks during and after diarrhoea found reductions in episodes of diarrhoea or respiratory disease in subsequent two to three months without additional Zinc supplements[17]. The lower rates of diarrhoea and acute lower respiratory infection in this and other studies indicate that a reduction in incidence could be due to a systemic effect of Zinc, probably through enhanced immune function. Several recent controlled trials have shown a preventive effect of routine Zinc supplementation on the incidence of diarrhoea. However, these studies provided daily Zinc supplementation for a period of 6-12 months, which is often not feasible in large scale programmes. Three studies in which Zinc was given for two weeks during and after diarrhoea found reductions in episodes of diarrhoea or respiratory disease in subsequent two to three months without additional zinc supplements. The lower rates of diarrhoea in this and other studies indicate that a reduction in incidence could be due to a systemic effect of zinc, probably through enhanced immune function. The reduction in hospital admissions for diarrhoea could have been due to effects of Zinc on episode duration, reduced incidence, or altered care seeking behaviour. A recent study from Bangladesh reported a higher prevalence of acute lower respiratory infection in Bangladeshi children in a six month follow up period after receipt of 20 mg elemental zinc daily for 14 days[18]. This may be due to environmental factors like poor socio-economic condition, seasonal flu or due to improper nutrition. The prevalence of acute lower respiratory infection was lower in children who received a 200, 000 IU vitamin A capsule after 14 days of Zinc supplementation. Studies evaluating the effect of Zinc supplementation on diarrhoeal diseases found a preventive and long-lasting impact. These showed that 10 mg to 20 mg of zinc per day, for 10 – 14 days, reduced the number of episodes of diarrhoea in 2 – 3 months after the supplementation[19]. This corroborates with the findings in our study. Shimelis D *et al* also concluded that, children who were given Zinc in the treatment of acute diarrhoea had their general well-being and appetite improved in the appetite scale[20]. A recently published randomised trial from India, found a large reduction in overall mortality in infants who were small for gestational age and supplemented daily with Zinc from 1 to 9 months of age. In India and Ethiopia, previous trials of long - term daily Zinc supplementation have documented positive effects of zinc supplementation among young infants and children[21,22]. Stunting rates, which are recommended indicators for high rates of zinc deficiency among children younger than 5 years, are high in India and Pakistan[23] and diarrhoea is frequent in children younger than 5 years[24]. Despite its benefits in diarrhoea management proven in many studies, there are several drawbacks that should be considered regarding the uncertainty of the long term effects of Zinc. Thus, advance research should be undertaken both in developed and developing countries through high quality study. The results from this study show that Zinc supplementation can improve diarrhoea management and that Zinc can reduce the duration and severity of diarrhoea in children. Comprehensive management in diarrhoea is absolute to achieve better outcomes. Comprehensive management consists of provision of safe drinking water, healthy sanitation, good nutritional status, adequate public education, selective antibiotics along with Zinc supplementation.

6. CONCLUSION

Zinc supplementation has an effective role in management of acute diarrhoea as such it shortens the duration of diarrhoea along with frequency of diarrhoea. Zinc supplementation, given at a dose of about 2RDAs per day (10-20 mg per day) for 14 days, is efficacious in reducing the severity of diarrhoea and the duration of the episode significantly. There is now enough evidence demonstrating the efficacy of zinc supplementation on the clinical course of acute diarrhoea. However, effectiveness studies to assess different strategies for delivering zinc supplementation to children with diarrhoea should be undertaken. These studies should investigate the feasibility, sustainability, and cost effectiveness of different zinc-delivery mechanisms, and monitor variables, such as consumption of ORS, antibiotic - use rate, non-diarrhoea morbidity, and overall mortality.

7. ACKNOWLEDGEMENT

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8. AUTHOR CONTRIBUTION STATEMENT

Dr Oinam Joychandra conceptualized the study, obtained permission for examining case - sheets and also provided valuable inputs for finalization. Dr Laitonjam Jonita collected the data and analysed it statistically. Dr Debashree Ningthoujam curated the data and drafted the manuscript. Dr Neerajkumar Sharma designed the tables and provided valuable inputs. All authors read and approved the final version of the manuscript.

9. CONFLICT OF INTEREST

Conflict of interest declared none.

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