

Efficacy of oral zinc as an adjuvant therapy in acute diarrhea in children aged 5-15 years

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Abstract

Introduction: Zinc as an adjuvant therapy in acute diarrhea has been proved effective in children aged below 5 years. Presently there are no any guidelines for the use of zinc in children above 5 years of age. So we studied efficacy of zinc as an adjunct therapy in acute diarrhea in children aged 5-15 years.

Materials and Methods: This hospital based longitudinal comparative study was conducted in D.Y.Patil medical college and hospital, Kolhapur, Maharashtra. 200 children aged 5-15 years, admitted with acute diarrhea with dehydration were included. 100 children received zinc (study group), orally 20 mg once a day for 14 days & another 100 were not received zinc (control group). Primary and secondary outcome measures in terms of frequency of loose stools per day at 24, 48 hours and on 7th day of admission and duration of hospital stay respectively were compared. The data was analyzed statistically.

Results: 75% & 25% children from study group and 27% & 69% from control group had frequency of loose stool ≤ 5 times and 6-7 times per day at 48 hours respectively. 3% and 78% children from study and 0% and 46% from control group had frequency of loose stool < 2 times and 2-4 times per day on 7th day respectively. In study group 88% children were discharged by 4th day and 76% from control group were discharged by 6th day with 2 days lesser hospital stay in children of study group. ($P < 0.001$)

Conclusion: Oral zinc as an adjuvant therapy was effective in acute diarrhea in children aged 5 -15 years.

Keywords: Acute diarrhea, Children, Zinc.

Introduction

Diarrhea is a one of the main cause of childhood morbidity and mortality in under 5 years olds affecting millions of children worldwide.^{1, 2} It is believed that 3.3 million deaths in developing countries occur each year is caused by diarrhea and contribute to malnutrition in surviving children.² Oral rehydration solution (ORS) has been used widely and effectively in acute diarrhea as per recommendation by World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNICEF).³ However, with the use of ORS, there is no change in stool volume, number of diarrheal days and frequency of loose stools, which raises a practical problem of its acceptance and compliance.⁴ Even use of probiotics like lactobacillus strain⁵ and anti-secretory drug like racecadotril⁶ were also studied and found some benefit as an adjunct therapy in acute diarrhea in children.

WHO and UNICEF now recommend a 10 to 14 day course of zinc and ORS for the treatment of acute diarrhea in children aged less than 5 years.^{7,8} Many studies have proved that zinc is effective as adjuvant therapy in acute diarrhea in children aged below 5 years.⁹⁻¹³ Presently, there are no any guidelines for the use of zinc in acute diarrhea as an adjunct therapy in children aged above 5 years. So in this study, we studied efficacy of zinc as an adjunct therapy in acute diarrhea in children aged 5-15 years in terms of reduction in frequency of loose stools per day and lesser duration of hospital stay.

Materials and Methods

This hospital based longitudinal comparative study was conducted in the Department of Pediatrics, D. Y. Patil Medical college and hospital, Kolhapur, Maharashtra during

the period of 1st September 2016 to 31st August 2018. The study was approved by Institutional Ethical Committee. Informed and written consent was taken from the parents/guardians.

200 children between 5-15 years of age who were admitted in inpatient department with acute diarrhea with some or severe dehydration were included in this study. Children suffering from malnutrition, acute bacillary dysentery, severe systemic illness and metabolic or endocrinal disorders were excluded from this study. Out of 200 children with acute diarrhea, 100 children received zinc (study group) & another 100 were not received zinc (control group). Zinc acetate was used as salt in the dose of 20mg once a day orally either in the form of either suspension (20 mg/5ml) or dispersible tablet for 14 days to children of study group. The compliance for zinc treatment was meticulously checked in children from study group.

Detailed history for diarrhea (frequency, duration, colour, volume and consistency), urine output and other complaints like vomiting, abdominal pain and fever were also asked from the parents/guardians. The clinical examination including vitals, general and systemic examination was done. Hydration status was assessed as some or severe dehydration and either ORS or intravenous fluid was administered for dehydration as per guidelines in children's from both groups.¹⁴ Children from both groups were also received lactobacillus strain, saccharomyces boulardii as probiotic from day 1 onwards in the same dose for 5 days. None of the children from both groups were received anti-secretory drug like racecadotril or anti-motility drug like loperamide. Relevant investigations like stool microscopy, culture and sensitivity, complete blood count, renal function test, urine routine microscopy were sent to

laboratory as per requirement.

Primary outcome measures in terms of frequency of loose stools per day at 24, 48 hours and 7th day of admission and secondary outcome measure in terms of duration of hospital stay were compared in both study and control groups. Those children who were discharged before 7 days, were given check-list to fill-up the frequency of loose stool per day on each day till 7th day at home and were followed up in Out Patient Department on 7th day. All the data was analyzed statistically by using Chi-square/ Fisher Exact test to find the significance of study parameters on categorical scale between two groups, where $p \leq 0.001$ was significant. The Statistical software SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data.

Results

Two hundred children with acute diarrhea aged 5-15 years, out of which 100 children received oral zinc (study group) & another 100 were not received zinc (control group). In this study, the incidence of acute diarrhea was maximum (72%) between 6-10 years of age and overall there was a male preponderance, 56% were males and 44% were females. Their age and gender distribution were shown in Table 1 and 2 and both groups were comparable statistically.

Table 1: Age wise distribution in study group and control group

Age in years	Study Group (N=100)	Control Group N=100	Total N=200	P value
≥5-10	71(71%)	73(73%)	144(72%)	0.951
>10-15	29(29%)	27(27%)	56(28%)	

Table 2: Gender distribution in both study group and control group

Gender	Study Group N=100	Control Group N=100	Total N=200	P value
Males	55(55%)	57(57%)	112(56%)	0.776
Females	45(45%)	43(43%)	88(44%)	

In this study children with severe dehydration were 24% and with some dehydration were 88%. [Table 3]

All 200 children, received intravenous fluids initially and then were switched over to ORS.

Table 3: Children with degree of dehydration in both study and control group

Degree of dehydration	Study Group (N=100)	Control Group (N=100)	Total (N=200)	P value
Severe dehydration	16(16%)	8(8%)	24(12%)	0.079
Some dehydration	84(84%)	92(92%)	176(88%)	

Children from both groups were followed up at 24 and 48 hours and till 7th day of admission. At 24 hours, there w

as no statistically significant difference in frequency of loose stools in both study and control group. [Table 4]

Table 4: Frequency of loose stools at 24 hours in both study group and control group

Frequency of loose stools/day	Study Group (N=100)	Control Group (N=100)	Total (N=200)	P value
5	5(5%)	3(3%)	8(4%)	0.524
6	23(23%)	20(20%)	43(21.5%)	
7	28(28%)	38(38%)	66(33%)	
8	34(34%)	27(27%)	61(30.5%)	
9	10(10%)	12(12%)	22(11%)	

At 48 hours, 75% and 27% children from study group and control group respectively had frequency of loose stools ≤ 5 times per day. 25% and 69% children from study group and control group respectively had frequency of loose stools 6-7

times per day. 4% children from control group were still having frequency of loose stools for 8 times per day as compared to none from study group. ($p < 0.001$) [Table 5.]

Table 5: Frequency of loose stools at 48 hours in both study group and control group

Frequency of loose stools/day	Study Group (N=100)	Control Group (N=100)	Total (N=200)	P value
4	18(18%)	3(3%)	21(10.5%)	<0.001
5	57(57%)	24(24%)	81(40.5%)	
6	22(22%)	47(47%)	69(34.5%)	
7	3(3%)	22(22%)	25(12.5%)	
8	0(0%)	4(4%)	4(2%)	

(P value is <0.001 significant.)

On 7th day of admission, 3% and 0% children from study and control group respectively had frequency of loose stools < 2 times per day and 78% and 46% children from study and control group respectively had frequency of loose

stools 2-4 times per day. The frequency of loose stool was significantly lower on 7th day in study group as compared with control group. (p < 0.001) [Table 6]

Table 6: Frequency of loose stools on day 7 in both study group and control group

Frequency of loose stools/day	Study Group (N=100)	Control Group (N=100)	Total (N=200)	P value
<2	3(3%)	0(0%)	3(1.5%)	<0.001
2	7(7%)	8(8%)	15(7.5%)	
3	34(34%)	16(16%)	50(25%)	
4	37(37%)	22(22%)	59(29.5%)	
5	9(9%)	31(31%)	40(20%)	
6	6(6%)	11(11%)	17(8.5%)	
7	2(2%)	7(7%)	9(4.5%)	
8	2(2%)	4(4%)	6(3%)	
>8	0(0%)	1(1%)	1(0.5%)	

(P <0.001 Significant)

In study group 88% children were discharged by 4th day of admission as compared to only 14% from control group where as 76% children from control group were discharged by 6th day. Children from study group had 2 days lesser hospital stay than children from control group which was

statistically significant.(P <0.001) Frequency of loose stools were decreased earlier significantly in study group than that of control group and thus lesser hospital stay, early recovery and early discharge in study group.[Fig. 1]

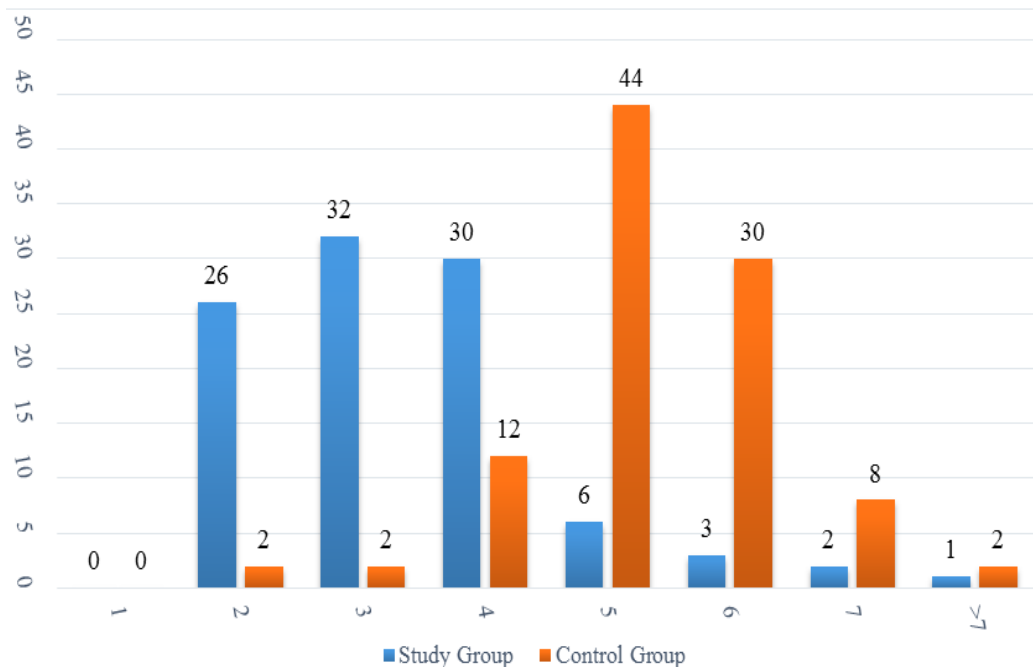


Fig. 1:Duration of hospital stay in percentage (%) in study group and control group

(p < 0.001 significant)

Discussion

Our study demonstrated that frequency of loose stools after 48 hours and on 7th day was significantly reduced, also duration of hospital stay was significantly less by 2 days in zinc received group. The use of zinc in acute diarrhoea and persistent diarrhea started later in 1990s. Many studies were done worldwide to know its efficacy, adverse reactions and interactions with other medications used in acute diarrhoea

such as ORS. In India first study of zinc supplementation in children with acute diarrhoea was done in 1995 by Sazawal

S. et al,⁹ where total 937 children with acute diarrhoea, aged 6 to 35 months, from New Delhi were studied and found that zinc supplementation resulted in reductions in duration and severity of diarrhea.

Lazzerini M et al,¹⁰ Nazarullah R et al,¹¹ Lukacik M et al¹² Lamberti M et al¹³ reported significant reduction in stool frequency and lesser duration of hospital stay in children with acute diarrhea who were supplemented with zinc in children less than 5 years. Surprisingly a study by Negi R et al¹⁵ found ineffectiveness of zinc as it did not shorten the duration of diarrhea or reduce subsequent episodes of diarrhea in 134 children for treating acute dehydrating diarrhea in 5-12 year old where they used 40 mg zinc.

How zinc exerts these therapeutic effects is not fully understood, even zinc is also effective in the absence of zinc deficiency. These could be possible mechanisms. Zinc is an essential micronutrient for human cell growth, differentiation, and DNA synthesis,¹⁶ and it is known to improve water and electrolytes absorption,¹⁷ early regeneration of the gut epithelium,¹⁸ increases brush border enzymes¹⁹ and enhance overall immune function.^{20,21} In animal rat studies, Hoque K M et al²² observed that zinc inhibits cAMP induced, chloride dependent fluid secretion by inhibiting basolateral potassium channels.

In our study, we did not find any adverse effects of zinc except vomiting in 3 children because of metallic taste, and still we continued oral zinc in suspension form for these 3 children along with food for better acceptance and tolerability. To date there were no severe adverse effects of zinc reported. A zinc dose of 40 mg has been approved as being safe to use by the Food and Drug administration (FDA) and zinc dosages of more than this can pose certain risks. Even there was no any evidence of short term zinc supplementation adversely affect the copper status.²³

This study had its own inherited limitations as it was purely observational based study. Secondly our study was a single centre study, before making any guidelines regarding use of zinc in children above 5 years, large, multi-centric study is needed.

Conclusion

Oral zinc as an adjuvant therapy was effective in the dose of 20 mg once a day in acute diarrhea in children aged 5 -15years of age in terms of significant reduction of frequency of loose stools lesser duration of hospital stay by 2 days.

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Conflict of Interest: None

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