

Comparative Evaluation on the Effect of Zinc-Probiotic and Zinc Therapy in Pediatric Acute Gastroenteritis

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Abstract

Background: Acute watery diarrhea in under 5 children is still a major health burden worldwide despite all available efforts that have been made to reduce its incidence and prevalence. Mortality rate is still high among under 5 children. Therefore, appropriate and comprehensive management of diarrhea is essential. There are lot of studies on the role of zinc and probiotic in reducing the duration and severity of acute watery diarrhea. This study emphasized on compared effect of using a combination zinc-probiotic and zinc in pediatric acute gastroenteritis.

Materials and methods: This was a randomized controlled trial type study, conducted at Department of Pediatric Gastroenterology at Chattogram Maa-O-Shishu Hospital Medical College from November 2018 to March 2019. A total of 100 numbers of children ages 3 months to 5 years with acute watery diarrhea were enrolled those who were fulfilled the selection criteria. They were divided into two groups. Group A (n=50) received zinc-probiotics combination therapy and group B (n=50) received zinc only. Measurement of disease severity was based on the frequency of diarrhea (Times/day) and duration of diarrhea (Hours) after initial drug consumption.

Results: Among the study population 63.5% male & 32.7% female in group A and 56.4% male & 34.5% female in group B. Duration of acute watery diarrhea was significantly reduced in group A than group B (56.4 hours versus 70.80 hours respectively). We also observed significant difference in length of hospital stay in Group A and Group B (68.16 hours vs 83.04 hours) respectively.

Conclusion: Combination therapy was more effective in reducing the severity of acute watery diarrhea than zinc alone therapy in under 5 children.

Key words: Acute watery diarrhea; Zinc; Probiotic; Outcome.

INTRODUCTION

Diarrhea remains the second leading cause of death among children 1-59 months of age¹. Currently, WHO recommends treatment with Oral Rehydration Salts (ORS) and continued feeding for the prevention and treatment of dehydration, as well as zinc to shorten the duration and severity of the episode². Probiotics are not recommended by WHO for the treatment of community-acquired acute diarrhea, though they are becoming increasingly popular in some countries³.

Probiotics are non-pathogenic live microorganisms. When ingested, probiotics can survive passage through the stomach and small bowel⁴. They compete with enteric pathogens for available nutrients and bacterial adhesion sites, increase the acidity of the intestinal environment, synthesize compounds that destroy or inhibit pathogens, and may stimulate the host's immune response to invading pathogens^{4,5}.

The use of probiotic nonpathogenic bacteria for prevention and therapy of diarrhea has been successful in some settings although the evidence is inconclusive to recommend their use in all settings⁶. Benefits of probiotics on diarrhea in children may be strain and/or etiology specific⁷⁻⁸.

Diarrhoea is more common in children with zinc deficiency and responds quickly to zinc supplementation. Zinc has a direct effect on intestinal villous, brush border disaccharides activity and intestinal transport of water and electrolytes. Zinc also has a marked effect on T cell function and its supplementation improves immunity. Thus it may also reduce the severity of diarrhea⁹⁻¹⁰.

Zinc administration for diarrhea management can significantly reduce all cause mortality by 46% and hospital admission by 23%⁶. A study of ICDDRB on Zinc supplementation in children with cholera in Bangladesh reveals that more patients in the zinc group than in the control group recovered by two days (49% v 32%, p-0.032) and by three days (81% vs.68%, p-0.03). Zinc supplemented patients had 12% shorter duration of diarrhea than control patients (64.1 vs. 72.8 h, P-0.028)¹¹. Zinc supplementation during acute diarrhoea is currently recommended by the World Health Organization and UNICEF¹².

So, we expect that combined therapy with zinc and probiotics will be more efficacious than zinc therapy alone. In this context our study is justifiable.

MATERIALS AND METHODS

We conduct an open, randomized, controlled trial from November 2018 to March 2019, in the Pediatric Diarrhoea Ward of Chattogram Maa-O-Shishu Hospital, Chattogram. We included children aged 3 months to 5 years with acute diarrhea. We excluded those with severe malnutrition, encephalitis, meningitis, sepsis, bronchopneumonia, immunocompromised state or stool culture positive cases. Subject were divided into two groups by simple randomization using random table. Group A received zinc sulfate 10mg/day for age <6 month and 20mg/day >6 month and probiotics two times orally for 10 days. Group 2 received zinc sulfate at the same dose as group B. The probiotics were mixed into milk or boiled water. Both doctor and parents were aware of the therapies given.

We did stool examination, stool culture positive cases excluded from study. Clinically the causes of diarrhea was distinguished by the stool consistency. Dysentery was characterized by acute diarrhea mixed with blood. We suspected cholera if symptom occurred during known diarrheal outbreak involving children and adults or frequent, voluminous, loose stool quickly led to severe dehydration with hypovolemic shock or severe dehydration occurred and antibiotics shortened the duration of diarrhea.

Monitoring of the duration and frequency of diarrhea was done during hospitalization on daily follow up, number of stool passed with consistency was recorded and sign of dehydration

was assessed. Presence of fever, vomiting, toxicity and side effects relating to the administration of zinc and probiotic were also observed. We defined recovery from diarrhea as stool passed <3 times with normal consistency. Home monitoring was done by contacting the parents or caregiver by mobile phone.

We used SPSS version 16 for data analysis. Independent t-test was used to assess the relationship between zinc-probiotic combination therapy and zinc alone as nominal scale with the duration and frequency of diarrhea as numerical scale. Difference were considered significant at a probability value of p<0.05 and 95% CI. Our study is an intention to treat analysis-based study.

RESULTS

There were 100 children who met the inclusion criteria. We divided them into two groups of 50 subject each: those who received zinc-probiotic combination therapy (Group A) and those who received zinc therapy alone (Group B)

Table I : Baseline characteristics

Characteristics	Group A Zinc-Probiotics n=50	Group B Zinc n=50
AGE (Month)		
Mean age ±SD in month	11.86 ±6.5	11.79 ± 5.98
3month to 6month	7 (13.5%)	10 (18.2%)
6month to 24month	40 (76.9%)	37 (67.3%)
24month to 59 month	3 (5.8%)	3 (5.5%)
Mean frequency of diarrhoea before treatment, times/day	10.93±10.27	12.25±10.35
Mean duration of diarrhea before treatment	58.4±18.67	52 ±23.5
Weight (Kg)	8.21±2.6	8.09±2.79
Male	33(63.5%)	31(56.4%)
Female	17(32.7%)	19(34.5%)
Breast feeding during 1st 6 month		
Exclusive breast feeding	31(59.6%)	32(58.2%)
Formula feeding	6(11.5%)	1(1.8%)
Mixed feeding	13(25%)	17(30.9%)
Water supply		
Tube well water	22(53.8%)	20(36.4%)
Supply water	28(42.3%)	30(54.5%)
Mothers education		
Above SSC	39(75%)	13(23.6%)
Below SSC	11(21.2%)	37(67.3%)
Knowledge about ORS preparation of mother		
knows	39(75%)	42(76.4%)
Dosen't know	11(21.2%)	8(14.4%)
Dehydration status		
No sign of dehydration	10(20%)	16(29.1%)
Some dehydration	40(80%)	34(61.8%)

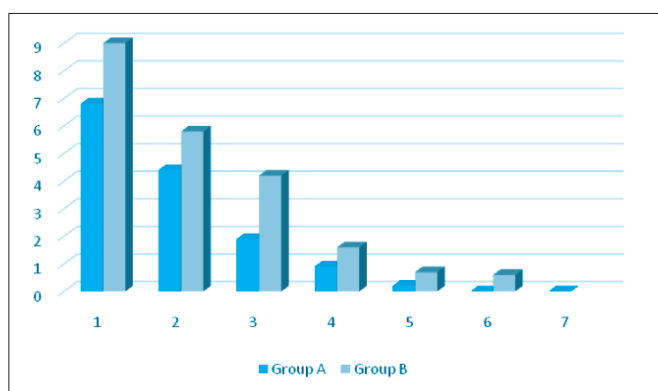


Figure 1: Frequency of diarrhea, time/day

The mean frequency of diarrhea before treatment was 10.93 times/day in the combination group, and 12.25 times/day in the zinc group. The duration of diarrhea before treatment was 52.8 hours (2.2 days) in the combination group and 57.6 hours (2.4 days) in the zinc group.

Table II : Duration of diarrhea and length of hospital stay after treatment

Characteristics	Group A	Group B	CI	p value
Duration of diarrhea (hours)	56.4± 21.36	70.8 ±22.8	-23.04 to -5.28	0.002
Length of hospital stay (hours)	68.16± 23.76	83.04± 26.16	-24.72 to -4.80	0.004

DISCUSSION

During treatment, there were significant differences in diarrheal frequency in the two groups from the first to fourth days. No parents or caregivers in either group reported recurrent diarrhea or complained of toxicity or side effects often associated with zinc and probiotics.

In this study, the mean age of children with acute diarrhea was 11.88±6.5 months in the combination group and 11.79±5.98 months in the zinc group. Previous epidemiological studies found that children with acute diarrhea were aged 0 to 12 months¹³. There was another study done by them where mean age was 19.18 ± 12.78 months & 20.02 ± 14.02 months in case & control group respectively¹⁴. There are more male in each group (63.5% vs 56.4%). One study of diarrhea in hospitalized children aged 0 to 36 months found that the incidence of acute diarrhea was higher in boys, but did not discuss possible theories for this occurrence. The incidence of diarrhea is more in between 6-24 month of age which is 40(76.9%) in group A and 37(67.3%) in group B respectively. Epidemiological study found that children with acute diarrhea caused by rotavirus were aged 0-12 month^{15,16}. The number of diarrhea patient in between 3-6 month is 7(13.5%) in group A and 10(18.2%) in group B respectively, but mostly around 75% are associated with mixed feeding. It is also observed that diarrhoea incidence is high who drink supply water and low socioeconomic group. In our study only 21.2% mothers in Group A and 14.4% mother

in Group B does not know how to prepare ORS, one of most important risk factor for electrolyte imbalance (hypernatremic and hyponatremic dehydration) which increase the mortality and morbidity in AWD in developing countries like Bangladesh.

Before admission, in this study, 10 (20%) 40 (80%) children in group A and 16 (29.1%), 34(61.8%) children in group B had no, and some dehydration respectively. Similar study done by Erdogan et al. where shown that 48% & 52% children in probiotic 1 (*Saccharomyces boulardii*) group, 44% & 56% in probiotic 2 (*Bifidobacterium lactis*) and 52% & 48% in control group (only oral rehydration) had no & some dehydration that is more or less similar to this study¹⁷.

Mean duration of diarrhea before treatment was 58.4±18.67 hours in combination group and 52 ±23.5 hours in zinc in our study. Aggarwal et al reported mean duration of diarrhea before treatment was 52.08 ± 30.48 hours in probiotic group & 59.52 ± 30.72 hours in control group. Duration of diarrhea before treatment was shorter than Aggarwal et al study¹⁷.

In present study on an average each patient passed 10.93±10.27 times of stool before treatment among the group A and 12.25±10.35 times of stool in group B. In this study, length of hospital stay was shorter in combination group than zinc group which is similar to Hatta et al study¹⁶.

Similar studies conducted by Billoo et al. Aggarwal et al. Azim et al also reported that probiotics improved consistency of stool^{17,18}.

Length of hospital stay cannot be used as an indicator of therapeutic success due to many other factors that affect the length of patient hospitalization, such as time delays in hospital discharge caused by the parents' requests or payment issues.

In my study zinc-probiotics group complete remission was achieved within 56.4±21.36 hours which was faster (p=0.002) than that of zinc alone group (70.8±22.8 hours). This study also showed a significant improvement in duration of hospital stay (68.16±23.76 hours VS 83.04±26.16 hours) in patients who were given in combination therapy.

LIMITATION

Limitation of this study were that the etiology of diarrhea was unknown and study was only admitted patients in the pediatric wards were enrolled which leads to selection bias.

CONCLUSION

World Health Organization (WHO) does not recommended the use of probiotic in diarrhea, but in our country the use of probiotic is increasing day by day in acute watery diarrhoeas. By doing this study we can conclude that, combination of probiotics & zinc therapy is more effective in reducing the severity of acute diarrhea than zinc therapy alone.

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DISCLOSURE

All the authors declared no competing interest.

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