

Comparison Between Therapeutic Efficacy of Zinc Only and Zinc-Probiotics in Children with Acute Gastroenteritis

Abdul Samad Kayani¹, Sara Asad², Tariq Saeed³, Haseeb Aslam⁴

¹PG trainee, Paediatric, Holy Family Hospital, Rawalpindi

²Consultant Gynecologist, Shifa International Hospital, Islamabad

³Professor of Paediatrics, Holy Family Hospital, Rawalpindi

⁴Medical Officer, Benazir Bhutto Hospital, Rawalpindi

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*E: analysis222@gmail.com

Introduction

Diarrhea is among the top three most common causes of child mortality^{1,2} contributing to an estimated annual death rate of 1.6 million globally.³ Despite key advancement in treatment modalities, childhood diarrhea factors majorly towards child mortality in underdeveloped countries such as Pakistan. As per WHO, an estimated 2.5 billion children below five years' experience episodes of diarrhea among developing and underdeveloped nations.⁴ Pakistan ranks number four in the top five countries contributing to cases and deaths due to diarrheal diseases. The reported prevalence of these diseases in Pakistan is five to six episodes per child annually and 500 deaths per day due to diarrhea.^{5,6}

The current guidelines of WHO for management of acute gastroenteritis include Oral Rehydration Solution and continued breast feeding to reduce mortality due to dehydration. In addition, zinc supplementations are recommended by both WHO and United Nations Children's Fund (UNICEF) for the treatment of childhood diarrhea.^{3,4} Although the use of probiotics in treating acute condition is no longer

ABSTRACT

Objective: To compare the efficacy of zinc supplements alone and in combination with probiotics for the treatment of acute gastroenteritis in children less than 5 years of age presenting to pediatrics OPD and Emergency Department of Holy Family Hospital, Rawalpindi.

Methodology: This comparative interventional study was conducted at the Pediatrics ward at Holy Family Hospital, Rawalpindi from Jul 2021 to Jan 2022. Hundred patients from Peds Emergency Department fulfilling the inclusion criteria, were selected by non-probability purposive sampling technique. Subjects were divided into two groups on the basis of treatment they are taking. Patients taking zinc sulfate with ORS placed in Group A while patient taking probiotics (*Bacillus clausii* 2B) along with ORS and zinc sulfate were placed in Group B. Assessment was done by checking stool frequency and grading of stools by using WHO criteria. Chi-square test was used to compare efficacy [grading of stool] among both the group. $P < 0.05$ was taken as significance.

Results: Mean age (months, years) in the study was 1.04+0.85 with majority female patients 61 (61.0%) and compared to male patients 39 (39.0%). Frequency and percentage of 4-7 no. of stools among both the groups 23 (46.0%) and 10 (20.0%) respectively.

Conclusion: The study concluded that Zinc with probiotic was more efficacious than zinc alone in treating acute diarrhea.

Key words: Supplements, Gastroenteritis, Zinc.

supported by WHO, they are still being prescribed in some settings.⁷ Probiotics are living microorganisms that are non-infective in nature. Once consumed, probiotics can persist through the channel to stomach and small intestine. Probiotics contend with enteric pathogens for spots of bacterial linkage and obtainable nutrients, increase levels of acidity in the intestines, produce compounds contributing to the destruction and obstruction of pathogens and could kindle the body's immune reaction to entering pathogens.^{8,9} Lack of minerals, specifically zinc, allegedly contribute to diarrhea in children and therefore zinc supplements are discovered to be effective in the prevention and improvement of diarrheal symptoms. Intake of zinc facilitates better immersion of electrolytes and water in the bowels, stimulates immune response, encourages epithelialization and upturns the amount intestinal enzymes, causing prompt dispersing of diarrhea.

Zinc supplements, consequently, may aid in decreasing of the span and intensity of diarrhea.^{10,11} Azim et al compared the efficacy of zinc supplements alone and in combination with probiotics and found

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an improvement in duration and frequency of diarrhea in children below 5 years. Similar results were reported by Sultana et al in their study. Ali. R studied the therapeutic effect of probiotics in childhood diarrhea and the results showed significant positive effect of probiotics. Ahmadipour concluded that zinc supplements played better role in treating acute diarrhea but probiotics can also be used depending on the type of diarrhea and probiotic species.¹¹ Kothari reported no beneficial effect of probiotics in acute cases of diarrhea among children.¹³ Worldwide, 68% of diarrheal disease occurs in young children. Diarrheal disease is the fifth leading cause of death in children worldwide, accounting for about 2.5 million deaths.

In the United States, acute gastroenteritis is not a major cause of death but leads to significant morbidity, especially in children younger than five years, accounting for 1.5 million office visits, 200,000 hospitalizations, and 300 deaths in children each year. The review focuses on acute gastroenteritis in children in industrialized nations, where viruses account for 75% to 90% of childhood acute infectious gastroenteritis. Approximately 20% of cases are due to bacteria. Diarrhea persisting for at least 14 days is more commonly caused by parasitic infections, which account for less than 5% of acute gastroenteritis cases. The specific causative microorganisms vary with season and climate.¹⁴ The increasing toll of high morbidity and mortality associated with diarrheal diseases in Pakistan warrants attention.

The aim of the study is to compare the effects of supplement that is zinc alone and with probiotics to determine any additional benefit of using probiotics on the mean duration and frequency of acute diarrhea in children of age between 6 months to 5 years. We expect that combined therapy with zinc and probiotics will be more efficacious than zinc therapy alone. Our study focuses on the therapeutic efficacy of probiotics in acute childhood diarrhea. The aim of the study is to compare the effects of zinc on their own and in combination with probiotics to determine any additional benefit of using probiotics on the mean duration and frequency of acute diarrhea in children of age between 6 months to 5 years.

Methodology

After the approval from ethical board review, a comparative interventional study was conducted in

Pediatrics ward at Holy Family Hospital, Rawalpindi. The duration of study was July 2021 to Jan, 2022. Total 100 patient were enrolled in the study with following WHO sample size calculations. Confidence interval:95%, Power of test: 80%, 50 patients in each group.⁸ Non probability purposive sampling technique was used for data collection purpose. Subjects were divided into two groups on the basis of treatment they are taking. Patients taking zinc sulfate with ORS was placed in Group A while patient taking probiotics (*Bacillus clausii* 2B) along with ORS and zinc sulfate was placed in Group B. Informed consent was taken from the parents after explaining them the complete procedure. Acute diarrhea is the occurrence of at least three evacuations of watery or loose stools, in 24 hours.

Assessment was done by checking stool frequency and grading of stools by using WHO grading criteria of stools, Grade I : Normal formed stools, Grade II : Soft stools, Grade III : Liquid stools containing the shape of container, Grade IV: Watery stools with flakes appears opaque in glass container, Grade V : Watery stools with few flakes, appears translucent in container. We include Children between 6 months to 5 years presenting with acute diarrhea whereas exclusion Criteria included patient with diarrhea that has received treatment of > 3(three) days at home, Critically ill child/ septicemia, Inflammatory or cardiac disease, non-cooperative, history of dysentery, mucoid diarrhea, use of antibiotics or anti parasitic medicines prior to admission and malnutrition, meningitis, septic shock, bronchopneumonia, encephalitis and immunocompromised child and positive stool cultures. Data was entered and analyzed through SPSS version 22. Frequency and percentage were calculated for qualitative variable like grading of stool, Mean and standard deviation were calculated for quantitative variables like frequency of stool. Chi-square test was used to compare efficacy [grading of stool] among both the group. $P < 0.05$ was taken as significance.

Results

Data was entered and analyzed in SPSS version 22.0. 100 patients fulfilling the inclusion criteria, were selected by non-probability purposive sampling technique. Subjects were divided into two groups on the basis of treatment they are taking. Patients taking zinc sulfate with ORS were placed in Group A

while patient taking probiotics (bacillus clausii 2B) along with ORS and zinc sulfate were placed in Group B. Mean age (months, years) in the study was 1.04±0.85. Majority were female patients 61 (61.0%) and compared to male patients 39 (39.0%), as shown in Table I.

Table II showed the analysis of efficacy of zinc supplements alone and in combination with probiotics for the treatment of acute gastroenteritis in children less than 5 years of age presenting to pediatrics OPD and Emergency Department of Holy Family Hospital, Rawalpindi. Frequency and percentage of 4-7 frequency of stools among both the groups 23 (46.0%) and 10 (20.0%) respectively. It showed Zinc with probiotic was more efficacious than zinc alone in treating acute diarrhea. Percentage of grade II of stools among both the groups 15 (30.0%) and 14 (28.0%) respectively, where percentage of grade III of stools among both the groups 18 (36.0%) and 12 (24.0%) respectively, which was statistically significant (0.014).

authors reported mean ages of 19.18 ± 12.78 months in the case group and 20.02 ± 14.02 months in the control group. There were more males in both groups (63.5% vs 56.4%). One study on diarrhea in hospitalized children aged 0 to 36 months found a higher incidence of acute diarrhea in boys, although it did not explore potential reasons for this difference.

The incidence of diarrhea was highest in children aged 6-24 months, with 40 (76.9%) in group A and 37 (67.3%) in group B. An epidemiological study also found that children with acute diarrhea caused by rotavirus were typically aged 0 to 12 months.¹⁶⁻¹⁷ 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 diarrhea 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 factors for electrolyte imbalance (hypernatremic and hyponatremic dehydration)

Table I: Descriptive statistics of Age & Gender.

		Probiotics	ORS+Zinc Sulfate	Total
Age (month, yrs)		1.05±0.87	1.03±0.84	
Gender	Male	18 (36%)	21 (42%)	39 (39%)
	Female	32 (64%)	29 (58%)	61 (61%)

Table II: Comparison of Frequency & Grading of Stools among both the groups.

		Probiotics	ORS+zinc Sulfate	Total	p-value
No. of stools	1-3	16 (32%)	32 (64%)	48 (48%)	0.012
	4-7	23 (46%)	10 (20%)	33 (33%)	
	8-10	9 (18%)	7 (14%)	16 (16%)	
	>10	2 (4%)	1 (2%)	3 (3%)	
Grading of stools	grade I	10 (20%)	21 (42%)	31 (31%)	0.149
	grade II	15 (30%)	14 (28%)	29 (29.0%)	
	grade III	18 (36%)	12 (24%)	30 (30.0%)	
	grade IV	5 (10.0%)	2 (4.0%)	7 (7.0%)	
	grade V	2 (4.0%)	-2.00%	3 (3.0%)	

Discussion

During treatment, significant differences in diarrheal frequency were observed between the two groups from the first to the fourth day. No parents or caregivers in either group reported recurrent diarrhea, nor were there any complaints of toxicity or side effects often associated with zinc or 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-only group. Previous epidemiological studies found that children with acute diarrhea were generally aged 0 to 12 months.¹³ Another study conducted by the same

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, 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 study.¹⁸

Mean duration of diarrhea before treatment was 58.4±18.67 hours in combination group and 52

± 23.5 hours in zinc in the study. It has been 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.¹⁸ 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.¹⁷ 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. Our study included 100 patients from Holy Family, Peads Emergency Department fulfilling the inclusion criteria, were selected by non-probability purposive sampling technique. Subjects were divided into two groups on the basis of treatment they are taking.

Patients taking zinc sulfate with ORS were placed in Group A while patient taking probiotics (bacillus clausii 2B) along with ORS and zinc sulfate were placed in Group B. Descriptive statistics were analyzed for age (months, years). In our study, mean age (months, years) in the study was 1.04 ± 0.85 .

Among 100 patients, majority were female patients 61 (61.0%) and compared to male patients 39 (39.0%). Frequency and percentage of no. of stools (4-7) among both the groups 23 (46.0%) and 10 (20.0%) respectively. It showed Zinc with probiotic was more efficacious than zinc alone in treating acute diarrhea. Grading of stools was assessed in the study. Percentage of grade II of stools among both the groups 15 (30.0%) and 14 (28.0%) respectively, where percentage of grade III of stools among both the groups 18 (36.0%) and 12 (24.0%) respectively.

Conclusion

The study concluded that Zinc with probiotic was more efficacious than zinc alone in treating acute diarrhea. This will contribute to decrease diarrhea related morbidity and mortality, speeding up hospital discharge and minimizing the burden on hospital economy due to prolonged hospital stay in our step.

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