

EFFICACY OF SACCHAROMYCES BOULARDII IN THE MANAGEMENT OF ACUTE WATERY DIARRHEA

Misbah Munir, Sajid Ali Shah*, Saeed Zaman**, Lutfullah Goheer***, Sana Bushra****, Sajjad Ahmad Khan*****

Mekran Medical College Turbat Pakistan, *Combined Military Hospital Skardu/National University of Medical Sciences (NUMS) Pakistan, **Combined Military Hospital Kharian/National University of Medical Sciences (NUMS) Pakistan, ***Combined Military Hospital Multan/National University of Medical Sciences (NUMS) Pakistan, ****Civil Hospital Quetta Pakistan, *****Fauji Foundation Hospital Peshawar Pakistan

ABSTRACT

Objective: To determine the Efficacy of probiotic (saccharomyces boulardii) in children (2 months to 5 years) with acute watery diarrhea.

Study Design: Comparative cross sectional study.

Place and Duration of Study: This study was carried out in the department of pediatrics, Combined Military Hospital, Quetta, from Jan 2017 to Jun 2018.

Methodology: All children (2 months to 5 years) with acute watery diarrhea presenting within 24 hour of illness with no dehydration and some dehydration were enrolled and divided into two groups, study group and control group. Efficacy was assessed by reduced frequency of stools (less than 3 per day) and duration during the study period.

Results: Mean age of the children in probiotic saccharomyces boulardii group was 3.42 ± 1.36 years, while mean age in control group was 3.91 ± 1.16 years (p -value 0.002). Significant difference was also observed in duration of stool and frequency of stool at day 1-5 (p -value <0.05). Statistically significant difference was observed among children in probiotic saccharomyces boulardii group 114 (53%) as compared to controls 101 (47%) (p -value 0.021).

Conclusion: The Efficacy of probiotic (saccharomyces boulardii) was found satisfactory in children (2 months to 5 years) with acute watery diarrhea. In children with acute watery diarrhea saccharomyces boulardii may be recommended for better outcome.

Keywords: Acute watery diarrhea, Children, Dehydration, Probiotics, Saccharomyces boulardii.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

As per World Health Organization (WHO) definition, stool emission with a frequency of 3 or more loose stool per day is termed as diarrhea. Quantification of stool in children especially in diaper babies may be difficult^{1,2}. Different mechanisms have been presumed for diarrhea. The final result of all the mechanisms is either increase in the volume of stool or there may be increase in stool frequency. Multiple factors are involved in water balance across the intestine mucosal membrane³⁻⁵. Diarrheal diseases are considered the fifth most leading cause of mortality in under 5 years children and the 8th leading cause of death among all ages, worldwide⁶. It is also the main cause of childhood mortality and morbidity in Pakistan: highest mortality from moderate to severe diarrhea reported from some part of Pakistan among south Asian countries^{7,8}.

Different etiological factors are involved in causing diarrhea. The most common cause of diarrhea is infection, with viruses top of the list. About 20% of infectious diarrhea is due to bacteria. Common strain of bacteria responsible for diarrhea are *E.Coli*, *Salmo-*

nella and *campylobacter* species etc. Besides bacterial infections, diarrhea may be caused by parasites and fungal infections. There are non-infectious causes of diarrhea as well like antibiotic associated diarrhea, diarrhea caused by toxins and some non-organic metals (Magnesium) etc. At time diarrhea may be a manifestation of systemic illness, particularly in children. Children with otitis media, encephalitis and pneumonia may present with loose motion. Route of transmission in most cases is oro-fecal. The spread of infections is due to unhygienic environment⁹. Infection may spread from person to person by direct contact or by taking contaminated food and water. The infection may remain localize to the intestine or may spread to other organs. The sign and symptoms then depend on the pathogenicity of the bacteria and the organ involved. The patients may present only with loose motion and vomiting or sometime may be having systemic symptoms as well like fever, malaise, respiratory and renal symptoms. Some organisms may result in fatal outcome, like *Clostridium difficile*, which may lead to life threatening colitis¹⁰.

We carried out our study with the aim to prove whether probiotics are efficacious in acute watery diarrhea or not. If proved to be efficacious, then

Correspondence: Dr Sajid Ali Shah, Department of Peads, Combined Military Hospital Skardu Pakistan

Received: 16 Jan 2020; revised received: 04 Nov 2020; accepted: 01 Apr 2021

probiotics would be recommended for acute watery diarrhea so as to decrease duration of disease, hospital stay and overall cost of the disease.

METHODOLOGY

This comparative cross sectional study was conducted in the department of Pediatric Medicine, Combined Military Hospital, Quetta, from Jan 2017 to Jun 2018. The sample size of 126 was required for each group. Sampling Technique used was non probability consecutive sampling. Inclusion criteria included Children (2 months to 5 years) with acute watery diarrhea presenting within 24 hour of illness with no dehydration and some dehydration. Children with severe inter-current illnesses, children with malnutrition, children with antibiotic associated diarrhea, children with chronic and persis-tent diarrhea, children with known food allergies and metabolic diseases, children with dysentery (blood and mucous in stool) and children with severe Dehydration were excluded from the study. Dehydration was classi-fied into no, some and severe on the basis of clinical symptoms (using integrated management of childhood illnesses). The following operational definitions were used.

Efficacy was labeled if frequency of stool (less than 3 per day) and duration of diarrhea decreases on 5th day as compared to controlled group.

Probiotic yeast (Saccharomyces Boulardii)

Acute watery diarrhea Passage of more than 3 loose stools per day.

Administrative permission from the concerned authorities and ethics committee was sought. Parents were explained about the risks and benefits of the study and informed written consent was obtained for examination of their children and intervention. Permission was also obtained from parents regarding use of data for research and publication. All those children, meriting inclusion criteria, were divided in two groups, study group and control group. The study group was managed with WHO standard therapy i.e. ORS plus oral administration of a probiotic Saccharomyces Boulardii (250mg in two divided doses less than three months and 250mg twice a day in infants more than 3 months) diluted in water around two teaspoon full or mixed with semi-solid food while the control group was managed with WHO standard therapy ORS alone. Efficacy was assessed by reduced frequency of stools (less than 3 per day) and duration on 5th day of the study period. Data regarding age and sex of patient and efficacy of treatment was recorded. Data was coll-

ected through a structured proforma. Confidentiality of the patient record was maintained.

All data was entered and analyzed using SPSS-21. Descriptive statistics was used to analyze and describe data. Frequencies were calculated for categorical (qualitative) variables. Mean and Standard Deviation (SD) were calculated for numerical (quantitative) variables. Efficacy was noted on 5th day of treatment. Chi-square test was applied to see the association of group with efficacy. Post stratification chi square test was also applied and p -value ≤ 0.05 was taken as significant.

RESULTS

Total numbers of patients in the study were 252 with 126 in study group and 126 patients in control group. Mean age of the children in probiotic sacchramyces boulardii group was 3.42 ± 1.36 years. while mean age in control group was 3.91 ± 1.16 years (p -value 0.002). Majority of the children were females, 134 (53.2%) as compared to males, 118 (46.8%). Mean weight of the children in probiotic sacchramyces boulardii group was 14.91 ± 4.14 Kg while mean weight in control group was 15.94 ± 3.22 Kg (p -value 0.029). Significant difference was also observed in duration of stool and frequency of stool at day 1-5. Overall efficacy was observed in 215 (85.30%) children. Efficacy was significantly higher 114 (53%) among children in probiotic sacchramyces boulardii group as compared to controls 101 (47%) (p -value 0.021) as shown in table-I.

Table-I: Efficacy with respect to group (n=252).

Group	Efficacy		p-value
	Yes	No	
Probiotic Saccharomyces Boulardii	114 (53%)	12 (32.4%)	0.021
Control	101 (47%)	25 (67.6%)	

Table-II: Age ≤ 3 years & Efficacy with respect to group (n=252).

Group	Efficacy		p-value
	Yes	No	
Probiotic Saccharomyces Boulardii	50 (69.4%)	0 (%0)	0.021
Control	22 (30.6%)	5 (100%)	

Table-III: Age >3 years & Efficacy with respect to group (n=252).

Group	Efficacy		p-value
	Yes	No	
Probiotic Saccharomyces Boulardii	54 (54.5%)	0 (0%)	<0.001
Control	45 (45.5%)	19 (100%)	

Stratification was done with respect to age and gender of the patients as shown in table-II-V.

Table-IV: Male Gender & Efficacy with respect to group (n=252).

Group	Efficacy		p-value
	Yes	No	
Probiotic Saccharomyces Boulardii	54 (54.5%)	0 (0%)	<0.001
Control	45 (45.5%)	19 (100%)	

Table-V: Female Gender & Efficacy with respect to group (n=252).

Group	Efficacy		p-value
	Yes	No	
Probiotic Saccharomyces Boulardii	60 (51.7%)	12 (66.7%)	0.237
Control	56 (48.3%)	6 (33.3%)	

DISCUSSION

Diarrhea is also classified as acute, persistent and chronic diarrhea depending on duration of onset. Similarly, diarrhea may be classified depending on stool characteristic like mostly watery, containing fats and having inflammatory cells etc. The most fearing aspect of diarrhea is dehydration, which occur if the fluid losses are not compensated. Dehydration may also result in fluid electrolytes imbalances, which then manifest in the form of different signs and symptoms^{11,12}.

In pediatric populations, over the past several years probiotics have been largely studied for treatment of diarrheal diseases. The probiotic is a living microorganism when administered proves to be beneficial for the health and wellbeing of host by interactions between immune cells and intestinal flora present in the intestinal mucosal barrier. The advantages are that it is, less invasive and have better efficacy. Various probiotic agents like Lactobacillus GG Lactobacillus Reuteri and Sacchomyces Boulardii have been used for the treatment of acute watery diarrhea. Saccharomyces boulardii has proven efficacy, from literature, in the treatment of acute diarrhoea with no adverse effects¹³.

Now a day the field of probiotics is of great interest for the researcher. New species of probiotic are being discovered and studied. The best probiotics, so far, studied are considered to be fungi. They have unique qualities. Fungi have specific cell structure which helps them to survive in the harsh gastrointestinal tract for a long period¹⁴. In pediatric populations, over the past several years probiotics have been largely studied for treatment of diarrheal diseases. Various

probiotic agents like Lactobacillus GG, Lactobacillus Reuteri and Sacchomyces Boulardii have been used for the treatment of acute watery diarrhea. Saccharomyces boulardii has proven efficacy, from literature, in the treatment of acute diarrhoea with no adverse effects¹⁴. In our study too we used saccharomyces boulardii as a probiotic. In this study, efficacy was significantly higher 114 (53%) among children in probiotic sacchramyces boulardii group as compared to controls 101 (47%) (*p*-value 0.021).

Acute diarrhoea is the most investigated disease in the area of probiotic use, especially in children and many systematic reviews described the probiotics role. Probiotics demonstrated a good safety profile, significantly reduction of diarrhoea duration, reduction of stool frequency and reduction of hospitalization period. A study done by Sharif MR enrolled 100 patients in each control and study groups. Both the groups were given standard treatment for diarrhea but the study group was given Sacchomyces Boulardii and the control group only placebo and no probiotics. The mother was asked about the duration and frequency of diarrhea every day after start of treatment. Significant improvement in term of frequency and duration of disease was reported in probiotic group as compared to control group¹⁵. Dinleyici *et al* studied the effectiveness of saccharomyces boulardii was studied in acute diarrhea patients reporting to emergency department, outdoor patients department and in admitted patients. The effectiveness was measured in term of frequency of stool, hospital stay and emergency department stay. Duration of diarrhea was significantly lower in probiotic group. Similarly, hospital stay and emergency department stay was also significantly lower in probiotic group as compared to control group. No adverse event was reported in probiotic group¹⁶.

The most studied diseases for probiotic use are acute diarrhea, diarrhea due do antibiotic use and necrotizing enterocolitis. But not all researchers agree with probiotic use for these diseases. Also, not all strains of probiotics may be equally effective. Conflicting results have been reported regarding probiotic use even for acute gastroenteritis. For necrotizing enterocolitis and antibiotic associated diarrhea further trials have been recommended before probiotic may be routinely advised in these conditions. Especially in our country where most of the time the diarrhea is due to infectious causes, probiotic should not be prescribed as a sole treatment¹⁷. Guarino *et al* review, regarding probiotic use for acute gastroenteritis, 7 studies did not recomm-

end probiotic use for gastroenteritis and 5 studies recommended its use. *Saccharomyces boulardii* and *Lactobacillus rhamnosus* were found to be the most effective strains to be used as a probiotics¹⁸.

All these studies and trials may provide understandings into the clinical application of probiotics, but it is important to elucidate the mechanisms of probiotics to maximize their health benefits. Limitation of our study was that we defined diarrhea clinically. We didn't went for stool culture. Similarly, we could not differentiate whether the watery diarrhea was infectious or noninfectious. We therefore recommend that further trials should be carried out which should elucidate the role of probiotics in infectious and non-infectious diarrhea.

CONCLUSION

The Efficacy of probiotic (*saccharomyces boulardii*) was found satisfactory in children (2 months to 5 years) with acute watery diarrhea. Probiotics may be prescribed to children with acute watery diarrhea as it decreases the severity of the disease.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any authors.

REFERENCES

1. Chu C, Rotondo-Trivette S. Chronic diarrhea. *Current Problems in Pediatric and Adolescent Health Care* 2020; 50(8): 100841.
2. Shah SA, Marwat SA, Rashid HU, Hussain A, Khurshid K. Importance of microscopic stool examination in patients with diarrhoea. *J Ayub Med Coll Abbottabad* 2014; 26(4): 478-80.
3. Roussel C, Sivignon A, de Wiele TV, Blanquet-Diot S. Foodborne enterotoxigenic *Escherichia coli*: from gut pathogenesis to new preventive strategies involving probiotics. *Future microbiol* 2017; 12(1): 73-93.
4. Xu Z, Zhong H, Zhou Q, Du Y, Chen L, Zhang Y, et al. A highly pathogenic strain of porcine deltacoronavirus caused watery diarrhea in newborn piglets. *Virology* 2018; 33(2): 131-41.
5. Radlović N, Leković Z, Vuletić B, Radlović V, Simić D. Acute diarrhea in children. *Srp Arh Celok Lek* 2015; 143(11-12): 755-62.
6. Troeger C, Blacker BF, Khalil IA, Rao PC, Cao S, Zimsen SR, et al. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of diarrhoea in 195 countries: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Infect Dis* 2018; 18(11): 1211-28.
7. Panwhar S, Fiedler BA. Upstream policy recommendations for pakistan's child mortality problem. In *Translating National Policy to Improve Environmental Conditions Impacting Public Health Through Community Planning*. Springer, Cham. 2018; 203-17.
8. Qamar FN, Zaman U, Quadri F, Khan A, Shaikh BT, Azam I, et al. Predictors of diarrheal mortality and patterns of caregiver health seeking behavior in Karachi, Pakistan. *J Glob Health* 2016; 6(6): 020406.
9. Rasool MH, Siddique AB, Saqalein M, Asghar MJ, Zahoor MA, Aslam B, et al. Occurrence and antibacterial susceptibility pattern of bacterial pathogens isolated from diarrheal patients in Pakistan. *Saudi Med J* 2016; 37(3): 274.
10. Kirk MD, Pires SM, Black RE, Caipo M, Crump JA, Devleeschauwer B, et al. World Health Organization estimates of the global and regional disease burden of 22 foodborne bacterial, protozoal, and viral diseases, 2010: a data synthesis. *PLoS Med* 2015; 12(12): e1001921.
11. Duplessis CA, Gutierrez RL, Porter CK. Chronic and persistent diarrhea with a focus in the returning traveler. *Trop Dis Trav Med Vaccin* 2017; 3(1): 9.
12. Das JK, Duggan C, Bhutta ZA. Persistent diarrhea in children in developing countries. In *Textbook of Pediatric Gastroenterology, Hepatology and Nutrition*. Springer, Cham. 2016; 195-202.
13. Ahmadi E, Alizadeh-Navaei R, Rezai MS. Efficacy of probiotic use in acute rotavirus diarrhea in children: A systematic review and meta-analysis. *Caspian J Intern Med* 2015; 6(4): 187.
14. Banik A, Halder SK, Ghosh C, Mondal KC. Fungal Probiotics: Opportunity, Challenge, and Prospects. In *Recent Advancement in White Biotechnology Through Fungi*. Springer, Cham 2019; 101-17.
15. Sharif MR, Kashani HH, Ardakani AT, Kheirkhah D, Tabatabaei F, Sharif A. The effect of a yeast probiotic on acute diarrhea in children. *Probiotics Antimicro* 2016; 8(4): 211-14.
16. Dinleyici EC, Kara A, Dalgic N, Kurugol Z, Arica V, Metin O, et al. *Saccharomyces boulardii* CNCM I-745 reduces the duration of diarrhoea, length of emergency care and hospital stay in children with acute diarrhoea. *Beneficial Microbes* 2015; 6(4): 415-21.
17. Quraishi F, Fatima G, Shaheen S, Memon Z, Kainat S, Agha F. In-Vitro comparison of antimicrobial actions of probiotics (*lactobacilli* species and *saccharomyces boulardii*) with standard antibiotics for the treatment of diarrhea in pediatric population. *Intl J Clin Med* 2018; 9(12): 827-40.
18. Guarino A, Guandalini S, Vecchio A. Probiotics for prevention and treatment of diarrhea. *J Clin Gastroenterol* 2015; 49(Suppl-1): 37-45.