ORIGINAL ARTICLE

Comparison of Multispecies Probiotic and Saccahomyces Boulardii in Children with Acute Watery Diarrhea in Terms of Mean Duration of Diarrhea

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ABSTRACT

Background: Acute watery diarrhea is a very common and sometimes fatal infectious illness, caused by a variety of bacterial, viral and parasitic organisms, the commonest being Rota virus. It accounts for approximately 1.5 million deaths per year globally. Although with the extensive use of ORS worldwide and institution of public health measures, the mortality associated with the diarrheal illness has decreased but the morbidity is still very high.
Objective: To compare a multispecies probiotic and Saccahomyces boulardii in children with acute watery diarrhea in terms of mean duration of diarrhea.
Design: It was a randomized controlled trial.
Study Settings: "Department of Neonatology, Pakistan Institute of Medical Sciences Islamabad for a period of six months i.e, 1st January, 2020 to 30th June 2020"
Patients and Methods: With age 6 months to 5-years of either gender, 300 hospitalized patients were divided into two groups by lottery method. After obtaining informed consent from the parents/guardians, patients in group A was treated with 1 sachet of saccharomyces boulardii twice daily for 5 days, in addition to WHO recommended therapies for diarrhea i.e. ORS and Zinc with nutritional support. While the patients in Group B were treated with 1 sachet of a multispecies probiotic twice daily for 5 days along with the WHO recommended therapies for diarrhea. In both groups clinical response to therapy was calculated in terms of days taken for resolution of diarrhea determined by decrease in frequency of defecation and improvement of stool consistency from watery to semi solid. However, the drug was labeled ineffective in cases where the patient had no response to above medicines and these patients were administered alternatilvey
Results: Mean age (yrs, months) of the patients in both the groups was 1.55+1.43 and 1.34+1.22 respectively. At presentation, mean duration of diarrhea in both the groups was 4.54+1.53 and 4.61+1.41 respectively, which was statistically not significant (p-value 0.653)/ Similarly, Mean duration of diarrhea at 5 day in both the groups was 2.60+0.87 and 2.71+0.86 respectively and it was not significant statistically (p-value 0.289).
Conclusion: It was held that there is no difference between multispecies probiotic and saccharomyces boulardii in treatment of acute watery diarrhea in terms of mean duration of diarrhea.
Keywords: Acute watery diarrhea (AWD), Probiotics, Saccharomyces boulardii.

INTRODUCTION

Acute watery diarrhea is a very common and sometimes fatal infectious illness, caused by a variety of bacterial, viral and parasitic organisms, the commonest being Rota virus.[1] Diarrheal diseases are the second foremost cause of mortality at childhood after pneumonia in children younger than 5 years of age.[2] It accounts for approximately 1.5 million deaths per year globally. And 80% of this disease burden is centered in South Asia and Africa.[3] Although with the extensive use of ORS worldwide and institution of public health measures, the mortality associated with the diarrheal illness has decreased but the morbidity is still very high.[4,5] It was recently reflected by "Demographic Health Survey of Pakistan [DHSP]" an average of 4 to 6 incidents of diarrhea per child under five years per annum; that if equated conservatively comes to above 100 millions episodes of diarrhea in children age under five years in each country.[6] Complications associated with acute watery diarrhea include prolongation of diarrheal episodes leading to malnutrition, secondary infections and micronutrient deficiencies. In developing countries, severe bacteremia, shock and DIC are some of the fatal complications in malnourished children with diarrhea.[7,8]

Probiotics are living microorganisms which if ingested in sufficient amount have positive health impact on host.6 Saccharomyces boulardii is a yeast probiotic, being used for prevention and treatment of various forms of gastrointestinal disorders including infectious diarrhea, traveler's diarrhea, antibiotic associated diarrhea, and inflammatory bowel disease.[9,10] The multispecies probiotic being used in this study contains Bifidobacterium BB 12, Lactobacillus casei and Streptococcus thermophilus which have been previously used in treatment of diarrhea alone as well as in combination[11,12].

In a study conducted in India, mean post intervention duration of diarrhea calculated was 52.08±24.57 hours in Saccharomyces boulardii group[4] while a similar study performed on Turkish children showed mean post intervention diarrhea duration was 77.9±30.5 hours in the group given a multispecies probiotic product. [5] A study conducted in Bolivian children, with a sample size of 20 per group, comparing a multispecies probiotic with Saccharomyces boulardii showed that median diarrhea

duration was 58 hours in the SB group and 60 hours in the multispecies group.[6]

As acute diarrhea is still one of the leading causes of morbidity, hospitalization and mortality in our country, a treatment option which can be helpful in decreasing the duration and severity of diarrhea merits further evaluation. Although probiotics are frequently being used in our local settings, but there was no consensus as to whether a single species probiotic is superior to a multispecies product. No local study has been done on the comparison of two products and international data is lacking in this context as well. Moreover, the international studies had a small sample size in majority of the cases. In this study a fairly large sample size was taken with a view that its results will help improved clinical outcome for routine use of this therapy.

PATIENTS AND METHODS

This randomized control trial was conducted at the Department of Neonatology, Pakistan Institute of Medical Sciences Islamabad for a period of six months i.e, 1st January, 2020 to 30th June 2020. Sample size of 300 patients was calculated with expected mean post intervention diarrhea duration was 77.9±30.5 hours in the group given a multispecies probiotic product at 80% power of test and 5% level of significance. [10] Patients were selected through Non-probability consecutive sampling from both the genders with age in the range of 6months to 5-years suffering from diarrhea less than 7 days. However, patients with bloody diarrhea, severe dehydration, severe electrolyte imbalance, immunocompromised children, and those with chronic diarrhea or malabsorption disorders and systemic illnesses (sepsis, pneumonia, urinary infections) and those who have already used antibiotics or probiotics during this illness were excluded from the study. Two equal groups were made through lottery method.

After obtaining informed consent from the parents/guardians, patients in group A was treated with 1 sachet of Saccharomyces boulardii twice daily for 5 days, in addition to WHO recommended therapies for diarrhea i.e. ORS and Zinc with nutritional support. While the patients in Group B were treated with 1 sachet of a multispecies probiotic twice daily for 5 days along with the WHO recommended therapies for diarrhea. The clinical response to the therapy in both groups were calculated in terms of number of days taken for resolution of diarrhea determined by decrease in frequency of defecation and improvement of stool consistency from watery to semi solid. Nevertheless if patient was not responding with medicines mentioned above, then the patients will be treated with alternate medicines till complete recovery of the patients and the drug was labeled as non-effective.

Data was entered and analyzed using SPSS Version 10.0. Descriptive stats were calculated for both qualitative and quantitative variables .Frequency and percentages was calculated for qualitative variables like gender of patients, consistency of stools. Mean and standard deviation was calculated for quantitative variables like age and duration of diarrhea (days). Independent sample t-test was used to compare the duration of diarrhea in both the groups. P<0.05 was taken as level of significance.

RESULTS

Mean Age (yrs, months) in Group A was 1.55+1.43, whereas mean age (yrs, months) in Group B was 1.34+1.22, as shown in Table 1. Frequency and percentages of male patients in both the groups was 90 (60.0%) and 68 (45.3%) respectively, whereas frequency and percentages of female patients in both the group was 60 (40%) and 82 (54.7%) respectively, as shown in Table 2.

The outcome of the study was to compare a multispecies probiotic and Sacchaomyces boulardii in children with acute watery diarrhea in terms of mean duration of diarrhea at presentation and at 5 days. Mean duration of diarrhea at presentation in both the groups was 4.54+1.53 and 4.61+1.41 respectively, which was statistically not significant (p-value 0.653). Similarly, Mean duration of diarrhea at day 5 in both the groups was 2.60+0.87 and 2.71+0.86 respectively, which was statistically not significant (p-value 0.289), as shown in Table3.

Table 1: Descriptive statistics of Age (yrs, months)

Age	N	Mean	Std. Deviation
(Yrs, Months)			
• Group A	150	1.55	1.43
• Group B	150	1.34	1.22

Table 2: Distribution of Gender of patients

Age / Gender	N	Total
Group A		
• Male	90 (60.0%)	150 (100.0%)
• Female	60 (40.0%	
Group B		
• Male	68 (45.3%)	150 (100.0%)
• Female	82(54.7%)	

Table 3: Comparison of Duration of Diarrhea at pre-post intervention in both the groups

Description	n	Mean	Std. Deviation	p-value
Duration of diarrhea (pre-intervention days at presentation)				
• Group A	150	4.54	1.535	0.653
• Group B	150	4.61	1.413	
Duration of diarrhea (post-intervention at day 5)				
• Group A	150	2.60	.871	0.289
• Group B	150	2.71	.868	

DISCUSSION

Increased loss of electrolytes and fluids in stool is called diarrhea. In infants, excessive loose stools of >10 mL/kg/day and in older children >200 g/24 hr lasting for <14 days is termed as acute diarrhea.[2] In children with age less than five years, second leading cause of death worldwide (18%) is diarrhea. Its annual episodes are 2.5 billion; resulting into 1.5 million deaths throughout the world and in Pakistan 500 deaths per day and its ratio is high in developing counters. Every child in Pakistan suffers from 5-6 diarrheal episodes on average per annum.[5] Depletion of salt and fluid is called dehydration which is a principal

danger to life. In infants less than one year, incidence of associated complications is very high. However, this diseased can not only be preventable but treatable as well. In its treatment, corner stones are rehydration and re-alimentation (ORS & continued feeding).[6,7] There is no controversy regarding benefits of rehydration and continued feeding. But rehydration therapy may not significantly reduce frequency and duration of diarrhea and for this reason the scientists have kept on looking for adjunctive therapies. Search for newer, safer and effective treatments continued after reporting of harmful effects of anti-cholinergic and anti-motility drugs. This led discovery and use of probiotics especially for preventions and treatments of gastrointestinal illnesses. Presently, for treating various conditions like gastrointestinal, respiratory and genitourinary infections, biological agents or "Probiotics" are being used. They are actually microbial cell components or preparations of microbial cells having beneficial effect on wellbeing and health of the hosts. As per latest definition given by FAO/WHO, probiotics are nonpathogenic live organisms conferring health benefits to hosts when adequately ingested. For managing diarrheal diseases, many probiotic agents have been studied that include Lactobacillus reuteri, Lactobacillus GG and S. boulardii.[15]

Currently numerous preparations of probiotics are available and are being used in clinical practice. Some of them are monostrain (containing a single probiotic strain of a certain species), some are multi strain (containing multiple strains of the same species), while others are multispecies products (containing strains belonging to more than one genera). Not much clinical data is currently available that shows the benefit of using a multispecies probiotic as compared to the one containing a single species or multiple strains of a single species. This study was thus designed to compare a multispecies probiotic and S. boulardii in children with AWD so that it can be concluded if one is superior to the other and should be recommended for regular use in clinical practice. No gender predilection was observed during the study as overall ration between male and female was 1:1. Our findings were consistent with already established ratio by Billo et al.[15]

Khan et al.[5] in their study found that the frequency and percentage of male patients in both the groups were 107(49.5) and 109(50.4) while female patients in both the groups were 103(50.4) and 101(49.5) respectively. Similarly, in our study, frequency and percentages of male patients in both the groups was 90 (60.0) and 68 (45.3) respectively, whereas frequency and percentages of female patients in both the group was 60 (40) and 82 (54.7) respectively.

Mainly children under age less than 2 years are more affected by the diarrheal disease.[16] These results were found matching with the results of current study where majority of the children had range less than 3-years. Another locally conducted study had also reported almost similar age range of 18.2 months.[15]

In our study, age (yrs, months) was calculated in terms of mean and standard deviation, with age ranges from 06 months to 05 years. Mean Age (yrs, months) in group A (treated with 1 sachet of Sacchaomyces boulardii) was 1.55+1.43, whereas mean age (yrs, months) in group B (1 sachet of a multispecies probiotics) was 1.34+1.22. Eren et al.[10] in their study found that mean and standard deviation of age in years was 24.4 ± 37.7 in group A (treated with Sacchaomyces boulardii) and 17.9 ± 12.5 in group B (treated with multispecies probiotics).

Malnutrition is also associated with cause and effect of diarrhea. In malnourished children, diarrheal condition gets even worse by atrophy of intestinal ville by aggravating malnutrition resultantly a vicious cycle of malnutrition and diarrhea starts. In nutritional subsets, no association of S.boulardii was found 38% children had dehydration while acute dehydration was found in 62%. Owing to variable degree of dehydration, it was not possible to statistically establish any correlation among them.[15] Findings of our study are further supported by Htwe et al.[17] who found no consistency in stool between two groups till day 2who were given ORS for five days with and without S.boulardii. However, on day three the ratio of returning to normal between cases and the controls was (76% vs. 24%) respectively. The duration of diarrhea in S. boulardii group was 3.08 days in comparison with the controls who had 4.68 days. Reduced duration of diarrhea along with shortened hospital stay in S. boulardii treatment group was shown by a systematic review.[18]

We did not find any significant differences between both the treatment groups with regard to number of stools after start of treatment within 24 hours. However, gradually after 48 hours onward, these results showed statistical significance in favor of probiotic group. At day 1, mean number of stools was comparable between both the groups. But at day 2-4, probiotic group had lower number of stools than the controls. Another study has also supported results of our study whose findings were mean number of stools per 24 hours, on day 0, (S. boulardii group 9.5 vs control group 8.8) and on day 3 (2.8 vs 4.4).[1] Another important outcome of the study was duration of diarrhea. In our study, probitoc group had mean duration of diarrhea for 3.43 days as compared to the controls with a reduction of 1.1 days than ORS group. Our findings have been supported by other studies with similar results.[15,16]

In a study comparing a multispecies probiotic with placebo, the duration of diarrhea was significantly shorter, approximately 36 h in children receiving the probiotic group than the controls (77.9 ± 30.5 vs. 114.6 ± 37.4 h, $p < 0.001$). The duration of hospitalization was shorter in children receiving the multispecies probiotic group (4.94 ± 1.7 vs. 5.77 ± 1.97 days, $p = 0.002$). The effect of probiotic mixture on diarrhea started after 24th hours and stool frequency significantly decreased after 24th and 48th hours.[9] In our study, mean post intervention duration of diarrhea in both the groups was 2.60+0.87 h and 2.71+0.86 h respectively. This shows no significant difference in the efficacy of both probiotics in treatment of acute watery diarrhea.

A limitation to current study was non-inclusion of patients with bloody diarrhea, severe dehydration, severe electrolyte imbalance, immunocompromised children, and those with chronic diarrhea or malabsorption disorders and systemic illnesses. That is why, in future such a study covering these variables is strongly recommended in future.

CONCLUSION

The study concludes that there is no difference between multispecies probiotic and saccharomyces boulardii in treatment of acute watery diarrhea in terms of mean duration of diarrhea. The study also proposed for conducting of further studies in the future for improving clinical outcome in terms of mean duration of diarrhea in order to get the evidence that either saccharomyces boulardii or multispecies probiotic therapy was better for routine use in patients with acute watery diarrhea.

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