Original Article

Efficacy of Saccharomyces Boullardii in Children with Acute Diarrhea

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ABSTRACT

Objectives: The main objectives of the study were to reduce the stool frequency, to improve the stool consistency and to reduce the mean duration of diarrhea in days.

Study Design: Prospective (case control) study

Place and Duration of Study: This study was conducted at Govt. Sifwat Ghayur Shaheed Memorial (infectious diseases) Children Hospital, Peshawar from May to Oct. 2016

Materials and Methods: A total of 200 patients were equally divided into two groups, cases and controls, randomly and consecutively. The cases group was receiving saccharomyces boullardii in addition to the routine management, while the control group was just receiving the normal management. Children of age, range between 6 months to 5 years were included in the study. Children with recurrent or chronic diarrhea, acute dysentery, thalassaemia and congenital heart disease were excluded of the study.

Results: The cases group had a mean duration of diarrhea of 3.23 days and control group 5.84 days. The difference in stool frequency, consistency and duration was statistically significant on day 3 between the two groups (0.008,0.000).

Conclusion: The use of saccharomyces boulardii is a beneficial addition to the management of acute diarrhea, which is associated with speedy recovery by improving stools frequency and consistency as compared to the patients who do not received.

Key Words: Efficacy, saccharomyces boulardii, dysentery, thalassaemia, congenital..

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INTRODUCTION

In children younger than 5 years of age after pneumonia, diarrhea is the second leading cause of morbidity and mortality.[1] In summer it accounts for (50-60%) of our hospital admissions. In Pakistan it causes an estimated 2.5 million deaths in children under 5 years of age per year which is very high as compared to the developed world.[2] Important factors increasing susceptibility to Diarrhea are lack of Breast Feeding, ingestion of contaminated food or water, exposure to unsanitary conditions, malnutrition, measles and level of maternal education. Saccharomyces boulardii is a tropical strain of yeast first isolated from lychee and mangosteen fruit in 1923 by French scientist Henri Boulard in Indochina and has been used as a remedy for Diarrhea since 1950.[3]

It has also shown to maintain and restore the natural flora in the large and small intestine; it is classified as a probiotic. It has been found to be more effective than the bacteria (lactobacillus) as a probiotic.[3] He observed natives of Southeast Asia chewing the skin of lychee and mangosteen to control the symptoms of cholera. It has been shown to be non-pathogenic, non-systemic (it remains in the gastrointestinal tract rather than spreading elsewhere in the body), and grows at the unusually high temperature of 37°C.[4]The mechanism of action of S. Boulardii is that it induces receptor competition. Increases mucin secretion or enhances probiotic induced action of gut associate lymph node tissue.[5]The use of saccharomyces boullardii in otherwise healthy children of aged $6m^0$ & 10 years showed significant decrease in reduced daily stool frequency on day 3 and 4 with increase in serum immunoglobulin A level and decrease in C-reactive proteins levels on day 7. Confirming the efficacy of S. Boullardii in paediatric acute Diarrhea and also enhancing the immune system response.[6]Studies from Mediline, embase cinahal and the conchrance liberary were obtained showing a significant improvement with the use of sacclaromyces boulardii in acute Diarrhea and also decreasing the risk of Diarrhea lasting more than 7 days.[7]S. Boullardii is a well tolerated drug with no side effects improving the stools consistency and the number of stools per day reduced to 2.7 and 4.2 respectively in cases verses controlled groups. The duration of Diarrhea was 3.6 days in S. Boullardii group whereas 4.8 in controlled group. [8] S. Boullardii was used as an adjunct to ORS in ambulatory care in children less than 2 years old with mild or moderate

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acute Diarrhea & reduced the risk of prolonged Diarrhea, with increased efficacy if started within the first 48 hours of commencement of Diarrhea.[9]A randomized controlled study showed that S. Boulardii is moderately effective in preventing antibiotic induced acute Diarrhea, showing that it is effective in any form of acute Diarrhea.[10] S. Boulardii is effective in the treatment of nosocomial Diarrhea and more so in sporadic and infectious Diarrhea showing the diverse nature of the drug and its use in different forms of acute Diarrhea.[11] Effective use of S. Boulardii could decrease patients exposure to antimicrobial.[12]S. Boulardii secures to be a promising agent for the amelioration of the course of acute Diarrhea in children when used therapeutically.[13]Probiotics are live microbial feeding supplements that beneficially affect the host animal by improving its microbial balance.[14] They are commonly used in the treatment and prevention of acute diarrhea. The rationale for using probiotics in acute infectious diarrhea is based on the assumption that they act against intestinal pathogens. However, the mechanism by which probiotics work is unclear. The possible mechanisms include the synthesis of antimicrobial substances[14,15], competition for nutrients required for growth of pathogens[14], competitive inhibition of adhesion of pathogens[16-17], modification of toxins or toxin receptors[18,19], and stimulation of nonspecific and specific immune responses to pathogens.Diarrhea is a common side effect of antibiotic treatment, especially among children. As many as 11-40% of children develop diarrhea while taking antibiotics. While no infectious microorganism is identified most of the time, a bacterium called Clostridium difficile is often the culprit underlying severe diarrheal episodes. To date, Ten[20] systematic reviews and meta-analyses have found probiotics effective at treating or preventing diarrhea.In 12 pediatric studies included in this analysis, probiotics reduced the likelihood of acute diarrhea in children by 57% ($p<0.001$). A 26% reduction of acute diarrhea was observed for adults.[21] Similar benefits were also obtained by others who found that probiotics reduced the risk of antibiotic-associated diarrhea from 28.5% with placebo down to 11.9%. In fact, it became apparent from an analysis that for every 7 patients that would normally develop diarrhea while taking antibiotics, one fewer person would get antibiotic-associated diarrhea if also taking a probiotic simultaneously.[22,23] The probiotics work against a type of E. coli bacteria that causes diarrhea by producing a chemical that is toxic to intestinal cells. Probiotics carry a molecule that looks a lot like the toxin receptor found on intestinal cells. This mimicry causes the toxin to bind to the microbes instead of the intestinal cells. Lab tests showed that these probiotics could bind and neutralize a significant amount of enterotoxin, according to a report in the medical journal Gastroenterology.[24]

MATERIALS AND METHODS

This was a prospective (case control) study of 6 months duration from May to Oct. 2016 conducted in Govt. Sifwat Ghayur shaheed Memorial (infectious diseases) children hospital Peshawar. A total of 200 patients were equally divided into two groups, cases and controls, randomly and consecutively. The cases group was receiving saccharomyces boullardii in addition to the routine management of acute diarrhea, while the control group was just receiving the normal management. Children of age range between 6 months to 5 years were included in the study, irrespective of their hydration status and present or past status of the use of antibiotics, and who could tolerate saccharomyces boulardii. Children with recurrent or chronic diarrhea, acute dysentery, thalassaemia and congenital heart disease were excluded of the study.

Arrival status of stool frequency and consistency, fever, level of consciousness, status of breast feeding and urine output was recorded on a predesigned and approved profarma and then the stool frequency and consistency were simultaneously checked on day1, 3, 5, and 7 respectively in both the groups.

Data Collection: The following variables will be studied:

1. Stool frequency: Will be a numerical variable.
2. Stool consistency: Will be a categorical variable.
3. Mean duration of diarrhea in days: Will be a numerical variable

Confounding variables: Type of feeding (whether bottle or breast),On arrival hydration status and usage of antibiotics would be our confounding variables and will be appropriately dealt with.

Data Analysis:

Descriptive Statistics: Descriptive statistics regarding the demographic and nominal data will be detailed with medians and/or means with standard deviations.

Test Statistics: Keeping in view the above variables under study, Unpaired T-test at 0.05% level of significance (p-value) will be used for comparison of the numerical variables like mean duration of diarrhea in days and the mean stool frequency in the two groups. Chi-square test will be used for comparison of proportion of patients having the stool consistency of less than Grade 3 in either of the two groups.

Statistical Software: SPSS 15, release 15.0.0, September, 2006; SPSS Inc. will be used for data entry and data analysis.

RESULTS

The study was conducted in Govt. Sifwat Ghayur Shaheed Memorial (Infectious diseases) children hospital Peshawar. A total of 234 patients were included, in which 21 patients prematurely discharged and 13 patients left against medical advice. In the remaining 200 patients, 100 were cases and 100

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controls. In the cases group 38(38%) were females and 62 (62%) were males, while in control group 44 (44%) were females and 56 (56%) males. The mean admission weight was 9.86 Kgs for cases and 11.6Kgs for control whose difference was not statistically significant. The average age of the cases group was 22.87 months and that of controls was 26.76 months with a standard deviation of 13.29 which was also not statistically significant. Regarding arrival stool frequency 92 (92%) cases and 94 (94%) controls had more than 10 episodes per day, and 8 cases (08%) verses 6 (6%) controls had episodes of 2-10 per day this was also not statistically significant (Table 1). Arrival stool consistency was uniformly same between the two groups and was more than grade 3.(Table1)The breast feeding status on arrival was that, 29 (29%) cases and 25 (25%) controls were exclusively breast fed, 36(36%) cases and 46 (46%) controls were partially breast fed, while 35 cases (35%) and 29 (29%) controls were bottle fed. The difference was also not statistically significant (Table 1). On admission 17 cases (17%) and 14 (14%) controls had mild dehydration, 57 cases (57%) and 66 (66%) controls had moderate, and 26 cases (26%) and 20 (20%) controls had severe dehydration, which was not statistically significant as well (Table 1). On arrival 56 cases (56%) and 47 (47 %) controls had fever which was also not statistically significant.(Table1).

Table No. 1: Arrival Status N=200

		Cases %	Controls %	Total	P. Values
Stool frequency	2-10 >10	8 (08) 92(92)	6(6) 94(94)	14 186	.500
Stool Consistency	>G3	100	100	200	.500
Breast Feeding Status	Exclusively Breast Fed Partially Br. Fed Bottle Fed	29(29) 36(36) 35(35)	25(25) 46(46) 29(29)	54 82 64	.512
Dehydration Status	Mild Moderate Severe	17(17) 57(57) 26(26)	14(14) 66(66) 20(20)	31 123 46	.600
Presence of fever	Yes No	56(56) 44(44)	47(47) 53(53)	103 97	.199
Urine output	Normal Decreased No	20(20) 67(67) 13(13)	13(13) 73(73) 14(14)	33 140 27	.692
Conscious level	Well oriented Irritable Comatose	19(19) 67(67) 14(14)	23(23) 63(63) 14(14)	42 130 28	.878

Table No. 2: Stool frequency and consistency N=200

			Cases %	Controls %	Total	P. value
Day 1	Stool frequency	3-10 >10	17(17) 83(83)	10 (10) 90(90)	27 173	.162
	Stool consistency	Grade 3 or below >grade 3	6(6) 94(94)	2(2) 98(98)	8 192	.183
Day 3	stool frequency	< 3, 3-10 >10	40(40) 50 (50) 10(10)	20(20) 52(52) 28(28)	60 102 38	.008
	stool consistency	Grade 3 or below >grade 3	63(63) 37(37)	32(32) 68(68)	95 105	.000
Day 5	stool frequency	<grade 3, 3-10 >10	77(77) 23(23) 0	44(44) 48(48) 8(8)	121 71 8	.000
	stool consistency	Grade 3 or below >grade 3	87(87) 13(13)	62(62) 38(38)	149 51	.000
Day 7	stool frequency	<grade 3 3-10 >10	98(98) 2(2) Nil	82(82) 18(18) Nil	180 20 Nil	.001
	Stool Consistency	Grade 3 or below >grade 3	94(94) 6(6)	85(85) 15(15)	179 21	.060

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Table No. 3: Independent sample t-test for equality of means in the duration of diarrhea between cases and controls

Stay	N	Mean Duration (in Days)	Std. Deviation	t-Value	df	Sig.(2-tailed)
Cases	100	3.23	1.309	-9.773	138	0.000
Controls	100	5.84	1.814		125.5	

On admission 20 (20%) cases and 13 (13%) controls had normal urine output, 67 cases (67%) and 73 (73%) controls had decreased urine output, while 13 cases (13%) and 14 (14%) controls had no urine output, with statistically no significant difference (Table 1). In the context of level of consciousness on arrival 19 cases (19%) and 23(23%) controls were well oriented, 67 cases (67%) and 63(63%) controls were irritable, and 14 cases (14%) and 14 (14%) controls were comatose. Again, statistically no significant difference (Table 1). On completion of day 1, 83 cases (83%) and 90 (90%) controls had stool frequency of more than 10 episodes per day, which was not statistically significant (Table 2).Regarding stool consistency also there was no significant difference between the two groups as 94 cases (94%) and 98 (98%) controls had more than grade 3 stool consistencies. (Table 2). On completion of day 3, 40 cases (40.00%) and 20 controls (20.00%) had stool frequency of less than 3 episodes per day, 50 cases (50.00%) and 52 (52.22%)controls had 3-10, and 10 cases (10.00%) verses 28 (28%) controls had more than 10 episodes of loose stools per day. Here the difference was Statistically Significant. (Table 2) Likewise stool consistency was also having statistically significant difference as 63 cases (63%) and 32 (32%) controls had grade 3 while 37 cases (37%) and 68 (68%) controls had more than grade 3 stool consistency. Same was the case on day 5 and day 7, there was uniform statistically significant difference between the two groups in terms of stools frequency and consistency. (Table 2) Use of antibiotics between the two groups did not have significant difference as well. The mean duration of diarrhea for cases was 3.23 days and controls were 5.84 days. (Table 3)

DISCUSSION

Acute Diarrhea is still one of the most common cause of mortality in our children. The disease burden is very high and in summer the admission may reach up to 25 to 30%. This study was carried out to determine the efficacy of S. Boulardii in children with Acute Diarrhea. Which showed an improvement of 3.23 days as compared to the other group. In Pakistan a study was done in children to assess the efficacy of Saccharomyces boulardii in acute watery diarrhea .This was randomized into group A (treated with ORS and nutrition appropriate for age) and Group B (treated with Saccharomyces boulardii 250 mg b.d. orally, ORS and nutrition appropriate for age). They were followed up for 6 days. Frequency and consistency of stool were recorded. There were 50 children in control (A) and 51 in study (B) group. The mean age was 17.45 months (range 3 to 60 months) . The frequency of stools on day 1 was the same in the two groups (P =0.175)). On day 3 the frequency reduced significantly in group B as compared to that of group A (P=0.02). The consistency of stool also improved as compared to control at day 3 (P=0.003) and day 6 (P=0.004) respectively. . This study was similar to ours, as it was done in the same age group and on third day results after the use of S Buolardii were the same as our study. But it was different as it was carried out in multiple centres and the number of patients were less than ours. Another study in Argentina was conducted to evaluate the efficacy of Saccharomyces boulardii as an adjuvant to ORS in shortening the duration of acute diarrhea in children. In a period of 1 year, 100 outpatients between 3 to 24 months presenting with acute mild to moderate diarrhea of less than 7 days duration were included in a double-blind, randomized, placebo-controlled trial evaluating the efficacy of S. boulardii administered for 6 days. 12 children were lost in follow-up; the data of 88 children could be analysed (44 in the placebo and 44 in the S. boulardii group).But 72 patients were followed for one month (37 in the placebo and 35 in the S. boulardii group) allowing the calculation of the duration of diarrhea. The mean duration of diarrhea was 6.16 days (range 2-13 days) in the placebo group and 4.70 days (range 2-10 days) in the S. boulardii group ($p<0.05$). On the 4th day, the patients in the S. boulardii group passed 2.5+/-1.4 stools/day versus 3.5+/-1.8 in the placebo group ($p<0.001$). A statistically significant difference was observed in the number of stools on 4th and 7th day in both groups. . This study was similar to our study because of improvement in diarrhea after the use of S.Boulardii but the age range was different and patients were studied for a longer duration of time. A study done in Myanmar to assess the effects of s.boulardii in Acute Diarrhea. One hundred hospitalized children in Myanmar age range (3 months to 10 years) were included. Fifty were treated with S. boulardii for five days in addition to ORS and 50 were given ORS alone (control group). The mean duration of diarrhea was 3.08 days in the S. boulardii group and 4.68 days ($P < 0.05$) in the control group. Stools had a normal consistency on day 3 in 38 (76%) of 50 patients in the S. boulardii group compared with only 12 (24%) of 50 in the control group ($P = 0.019$). On day 2, 27 (54%) of 50 had less than three stools per day in the S. boulardii group compared with only 15 (30%) of 50 in the control group ($P = 0.019$). Saccharomyces boulardii shortens the duration of diarrhea and normalizes stool consistency and frequency. This study was similar to our study in terms of the improvement in diarrhea but the age group was different and patients were not observed for 7 days.

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CONCLUSION

In children Acute diarrhea is a common admitting diagnosis and a major cause of morbidity and mortality. The use of saccharomyces boulardii is safe and has clear beneficial effect which is associated with speedy recovery. It improves stool frequency, consistency, reduce hospital stay and of great importance is, its anxiety relieving effects of parents because early recovery of their children.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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