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ACUTE DIARRHEA;
ROLE OF SACCHAROMYCES BOULARDII IN THE TREATMENT

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ABSTRACT… Acute diarrhea is the fourth-ranking cause of death in children under the age of 5 years. after neonatal causes, malaria, and acute respiratory infections. **Objectives:** To determine the role of Saccharomyces boulardii in the treatment of acute diarrhea. **Design:** Comparative study. **Period:** Six months, Mar to Aug 2013. **Setting:** Pediatric Unit II- Liaquat University Hospital Jamshoro/ Hyderabad. **Patients and methods:** It consisted of 100 patients, of acute diarrhea with age between 3 months to 5 years reported to pediatric unit and fulfilled the inclusion criteria. Cases were given low osmolar ORS, Zinc & Saccharomyces boulardii 250mg twice daily for three days and controls were given low osmolar ORS and Zinc. P-value ≤0.05 was considered as significant. **Results:** The results showed that 51 patients were male and 49 patients were female. 27 male patients were in control and 24 were in case group. 23 female patients were in control and 26 were in case group. The overall mean age of study subjects was 26.73±12.65 months. Among reported patients most of the patients 84% were reported on 1st day. All reported patients had a complaint of loose motion with 73% also had vomiting. All patients had watery loose motion. The mean duration was 4.20±1.70 days with the mean frequency of 9.82±6.16 times. Among the patients 96 patients were hospitalized and 97 patients were given I/V fluid. Among reported patients 10 were without dehyderation, 8 had some dehyderation, and 82 had severe dehyderation. 52 had acceptability of probiotics. The results were evaluated according to 1st, 2nd, and 3rd day post intervention. Among 50 patients of case group, 18 patients were compliance. 49 patients had decrease in duration. The same results were observed in the decrease in frequency. Consistency was improved in 39 patients. The duration of hospitalization was reduced in 36 patients. It was observed that improvement in the duration, frequency, and consistency was mostly observed on 2nd day of post intervention. **Conclusions:** The role of S. boulardii as a good biotherapeutic agent allowing to prevent and/or treat several grastrointestinal diseases. In comparison to probiotic bacteria, the use of probiotic yeast is beneficial when the treatment is combined to antibiotherapy.

Key words: Diarrhea, Acute Diarrhea, Probiotics, Dehydration, Osmolar ORS, Saccharomyces Boulardii

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INTRODUCTION

Acute diarrhea is the fourth-ranking cause of death in children under the age of 5 years, after neonatal causes, malaria, and acute respiratory infections[1]. Diarrheal diseases causes 1.5 million annual deaths globally (500 deaths per day in Pakistan)[2]. Most of these deaths occur in developing countries. In Pakistan, every child on average suffers from 5-6 episodes of diarrhea per year[3]. The reported prevalence of diarrhea in Punjab is found as 7.8%[4]. Dehydration (fluid and salt depletion) remains the principal danger to life. Incidence of complications is highest in infants (one month to 1 year) [2,4].

Recently, the World Health Organization (WHO) recommended the use of rotavirus vaccines worldwide for acute diarrhea however, WHO recommendation in 2004 to use zinc for the treatment of acute diarrhea in children[5]. Probiotics may offer an attractive supportive therapy along with oral rehydration solution (ORS) recommended by WHO[6] for treatment and prevention of acute diarrhea in children[7].

Numerous probiotic substances (lactobacillus GG, lactobacillus reuteri and S. boulardii) have been studied for management of diarrheal diseases[8]. Two main probiotic strains, lactobacillus GG and Saccharomyces boulardii (S. boulardii)[9,10]

have been best documented. The efficacy of S. boulardii in the management of gastroenteritis has been shown in several clinical trials in developing countries. Saccharomyces boulardii act by inhibiting the pathogen adhesion, strengthening of enterocyte junctions, neutralization of bacterial virulence factors and increased mucosal immune response.[11-17]S.boulardii effectively reduces the risk of antibiotic-associated diarrhoea[18].

The published data from developing countries like Pakistan is limited. Extensive further research is required to accept treatment with probiotics to reduce the undesirable morbidity. As multiple studies on efficacy combining Saccharomyces boulardii along with other probiotics have been conducted with varying results but limited studies available showing the efficacy of only Saccharomyces boulardii. This study assessed the efficacy of Saccharomyces boulardii for treating the children with acute diarrhea and can be beneficial in adding on to pre-existing data. The objective of this study was to determine the role of Saccharomyces boulardii in the treatment of acute diarrhea.

PATIENTS AND METHODS

Total 100 patients of either sex were included in the study. They were divided in two groups i.e. cases and controls. Each group was allotted 50 patients. The babies aged 3 months to 5 years, regardless of sex presenting with loose motion < 14 days duration were included in this study while the exclusion criteria were babies who will be severely malnourished, babies having blood in stools and those with poor adherence to treatment. The children aged 3 months to 5 years reported in pediatric department LUH Hyderabad who fulfill the inclusion criteria were enrolled for the study. After taking written and informed consent, data was collected on proforma embodying related clinical history, examination and response to treatment. After correction of dehydration status by giving I/V fluids for severe dehydration and low osmolar ORS for some dehydration, patients were divided randomly into two group i.e. cases and controls. In order to review efficacy, one group were given low osmolar ORS, Zinc & Saccharomyces boulardii 250 mg twice daily for three days (cases) and other group (controls) were given low osmolar ORS and Zinc. Question regarding duration, frequency and consistency of stools were asked from primary caregiver. The data for all enrolled babies were analyzed using SPSS-version 17(statistical package for social sciences). Chi-square test was applied for categorical variables. Primary outcome variables in this study were duration, frequency, consistency of stools and duration of hospitalization and secondary outcome variables were vomiting and adherence to treatment. Mean values of outcomes, standard deviation of outcomes and number of babies assessed for outcome were extracted. P-value ≤0.05 was considered as significant.

RESULTS

Total 100 patients of either gender with age between 3 months to 5 years were evaluated to determine the role of probiotics for treating acute diarrhea, of which 51 were males and 49 females. The patients were classified with control and case groups. In case group, patients were given low osmolar ORS, Zinc & Saccharomyces boulardii 250 mg twice daily for three days and patients in control group were given low osmolar ORS and Zinc. The overall mean age of study subjects was 26.73±12.65 months (Graph-2). Among male patients, mean age of study subjects was 25.61±12.48 months. Among female patients, mean age of study subjects was 27.90±12.85 months (Table-I).

	Age	Gender	
	Overall	Male	Female
Mean ±SD	26.73±12.65	25.61±12.48	27.90±12.85
Median	24	24	30
Min - Max	7 – 60	7 – 60	8 – 54
Range	53	53	46

Table-I. Descriptive statistics of overall age (months) and according to gender

Among reported patients most of the patients 84% were reported on 1st day, 11% patients were reported on 2nd day and only 5% patients were reported on 3rd day. All reported patients had a complaint of loose motion with 73% also had vomiting. All patients had watery loose motion.

Among reported patients 10 were without

dehyderation, 08 had some dehyderation, and 82 had severe dehyderation. 52 had acceptability of probiotics. Because all reported patients had a complaint of loose motion they were divided equally i.e. 50 in each group. Among 73 patients who had vomiting, 37 were in control group and 36 were in case group. Because all reported patients had a complaint of watery loose motion they were divided equally i.e. 50 in each group. Among the 96 patients who were hospitalized, 48 were in each group. Among 97 patients who were given I/V fliud, 50 were in control and 47 were in case group (Table-II).

	Control (50) n (%)	Case (50) n (%)
Loose Motion	50(100)	50(100)
Vomiting	37(74)	36(72)
Consistency (Watery)	50(100)	50(100)
Hospitalization	48(96)	48(96)
I/V Fluid Given	50(100)	47(94)

Table-II. Descriptive statistics of according to presentation and treatment

In Case group the effect of Saccharomyces Boulardii on acute diarrhea was evaluated and the results were recorded interms of decrease and no effect. The results were evaluated according to 1st, 2nd and 3rd day. Among 50 patients of case group, 18 patients were compliance. 49 patients had decrease in duration. The same results were observed in the decrease in frequency. Consistency was improved in 39 patients. The probiotics were not such effective to reduce the duration of hospitalization. The duration of hospitalization was reduced in 36 patients (Table-III). It was observed that improvement in the duration, frequency, and consistency was mostly observed on 2nd day of post intervention Fig-1.

(n=50)	Decreased n (%)	No Effect n (%)
Compliance	18(36)	32(64)
Duration	49(98)	1(2)
Frequency	49(98)	1(2)
Consistency	39(78)	11(22)
Duration of Hospitalization	18(36)	32(64)

Table-III. Frequency distribution for effectiveness of probiotics

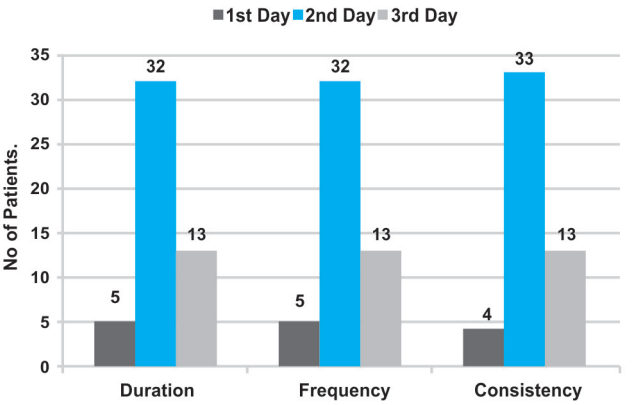

Fig-1. Percentage of patients improved in days

DISCUSSION

Diarrhea is both a cause and effect of malnutrition Diarrheal diseases mainly affect children under 2 years of age. In recent study, the age range of tested populace was 2 months to 5 years with a mean at 19.2 months. Almost half of the children were infants with overall majority (90%) less than 3 years. These results showed majority of children belonged to age up to 3 years. Mean age of the studied children was comparable with local study having mean age 18.2 months[3,4].

The current definition by FAO / WHO suggest probiotics as nonpathogenic live microorganisms that provide beneficial effects on the health of the host[19-21].

A randomized controlled trial was conducted by Htwe and colleagues in children with AWD[22]. The children received ORS with and without S. boulardii, (250 mg twice daily) for 5 days. Stool consistency showed no difference between the two groups on day. But on day it returned to normal in 76% of active treatment[22]. Regarding stool frequency on 2nd day, 54% children of the treatment group were observed passing less than 3 stools per day as compared to thirty percent in control group. The mean duration of diarrhea was 3.08 days in S. boulardii group as compared to 4.68 day of control group. This study supports our results regarding clinical efficacy of probiotics in children with AWD.

In our study, the effect of Saccharomyces Boulardii on acute diarrhea was evaluated and

the results showed that among 50 patients of case group, 49 patients had decrease in duration. The same results were observed in the decrease in frequency. Consistency was improved in 39 patients. It was observed that improvement in the duration, frequency, and consistency was mostly observed on 2nd day of post intervention.

There was no significant difference between the two groups regarding the mean number of stools after 24 hours of beginning of treatment. However, the results showed statistically significant gradual reduction in favor of probiotic group from 48 hours onwards. The mean number of stools remained comparable between probiotic group and control group on day 0 and day 1. However in probiotic group the mean number of stools was lower on day 2, day 3 and day 4 compared to control group 2. These results were comparable with another study regarding 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).[3] Similarly in another study, after the second day of treatment the median stool frequency was significantly low in S. boulardii group than in the control group[23]. The results of our study were comparable with all these study regarding decrease in mean number of stools per 24 hours.

The duration of diarrhea i.e. time from start of treatment until the appearance of first normal stool was an important outcome. The overall assessment of clinical response showed a remarkable reduction in mean duration of diarrhea in S. boulardii group than ORS group. The mean duration of diarrhea in probiotic group was 3.43 days compared to control group. Hence the probiotic group had shown a reduction in duration of diarrhea by 1.1 day compared with the ORS group. This is consistent with our study and as well as the results found in a number of other studies.[24]In fact they have entered mainstream and duration of infectious gastroenteritis[25].

There is published data, which showed that S. boulardii had no or little clinical effect on diarrhea in children[26]. The study did not document the age and nutritional status of the children. These variables may have some correlation with the effect of probiotics. Another study conducted in Turkey showed the duration of diarrhea as significantly reduced (more than one day) in S. boulardii group compared with placebo Probiotic group in children having acute diarrhea[27].

Our results clearly show that S. boulardii had reduced the mean duration of diarrhea, as well as frequency of stools and improved the consistency of stools. Although no clear effect of S. boulardii was determined between the two groups regarding their nutritional status and degree of dehydration, S. boulardii is beneficial by promoting general well being. Villaruel et al demonstrated a mean difference of 1.37 days in duration of diarrhea in a group of 88 children from Salta (Argentina) treated with S. boulardi compared to placebo, also, the number of children with prolonged diarrhea (>7 days) was significantly higher in the placebo groyp (52.2 % versus 20.4 %; RR 0.39 (0.20-0.74) [28]. Kurugol and coworkers studied 200 Turkish children with acute diarrhea, and showed a decreased duration of diarrhea (7 + 2.5 versus 5.5 +3.2 days; $p = 0.03$) and shorter hospital stay (2.8 + 1.1versus 3.8 + 1.4 days; $p < 0.001$)[27].

The mean duration of diarrhea in children treated with S. boulardi in study was slightly shorter, 2.5 days. Probiotics can be used as "add-on treatment" to ORT and rapid re-alimentation in children and infants with acute diarrhea. S. boulardii was well tolerated, as no side effects were observed[1]. The mean duration of diarrhea in children treated with S. boulardi in this study was slightly shorter, 2.5 days. Probiotics can be used as add-on treatment to ORT and rapid re-alimentation in children and infants with acute diarrhea. S. boulardii was well tolerated, as no side effects were observed.

CONCLUSIONS

S. boulardii role in the prevention and treatment of diarrhea had been widely demonstrated. However, new advance clinical studies should be conducted to determine the mechanisms of action of the yeast and its therapeutic role.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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1	Dr. Farzana Shaikh	Review literature and compile results	
2	Dr. Sikandar Ali Bhand	Helping in collecting data	
3	Dr. Parkash Kumar	Compile results	
4	Prof. Mohammad Akbar Nizamani	Review the manuscript	