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The Effect of a Yeast Probiotic on Acute Diarrhea in Children

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Abstract A probiotic is a living micro-organism administered to promote the health of the host by treating or preventing infections owing to strains of pathogens. *Saccharomyces boulardii* is a nonpathogen yeast that has a direct inhibitory effect on the growth of many pathogens, an anti-secretory effect and a trophic effect on enterocytes. The aim of this study was to determine the effect of *S. boulardii* on diarrhea in children. The children from 6 months to 6 years of age with acute watery diarrhea admitted in pediatric clinic in Kashan in 2012 were included in this trial. Exclusion criteria were high fever ($T > 38.5$ °C), severe dehydration, bloody diarrhea, severe malnutrition, using of antibiotics, anti-diarrheal or anti-fungal drugs and children with more than one complain. Two hundred patients were assigned into two groups: A total of 100 patients were treated with *S. boulardii* in addition to ORS (case group) and 100 patients were given placebo in addition to ORS (control group). The duration of diarrhea and frequency of stools were recorded by asking the mothers of the children every day. The results showed that the defecation frequency after second day of treatment in the case group was significantly less than the control group ($P = 0.001$) and the mean numbers of days of diarrhea was significantly lower in the case group ($P = 0.001$). The result of this study confirms that *S. boulardii* reduces the frequency of stool and duration of illness in children.

Keywords Acute diarrhea · Children · Probiotic · *Saccharomyces boulardii* · Yeast

Introduction

Diarrhea is a common manifestation of many gastrointestinal diseases. It means as a decrease in fecal consistency and occurs when there is an imbalance between water and ions intestinal absorption and secretion. Diarrheal diseases are the most common health problems in the developing countries and the first cause of hospitalization in children [1]. Treatment of diarrhea basically consists replacing of lost fluids by means of oral rehydration solution (ORS) [1–3]. The use of ORS in diarrhea reduces the rate of mortality and morbidity of the disease but does not lead to the decrease in the duration of diarrhea and its intensity [4–7]. Testing different strategies to help in this direction, probiotics appear as one of the alternatives currently under discussion that may shorten the duration of diarrhea [4, 8]. The use of yoghurt (as a probiotic) in the treatment of diarrhea has been known for a long time ago [9].The United Nations and World Health Organization define probiotics as "Live micro-organisms which when administered in adequate amounts confer a health benefit on the host" [9, 10]. Probiotics promote the health of the host by treating or preventing infections owing to strains of pathogens [9]. A few agents, including *Lactobacillus GG*, *Lactobacillus reuteri* and *Saccharomyces boulardii,* seem to be promising agents for the amelioration of the course of acute diarrhea in children [9, 11]. Among these, all are bacteria except *S. boulardii* which is yeast [9].

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Saccharomyces boulardii is a nonpathogenic, nontoxic yeast strain. It is the tropical yeast found in a permanent unicellular state, a eukaryote of the order endomycetales [12]. It was first described in 1920 by the microbiologist Henri Boulerd, who isolated the yeast from the skins of lychee nuts from his travels in Indonesia [10, 13]. After he had observed, it was eaten as an anti-diarrheal agent by the local population [9, 12]. The yeast, which now bears his name, is a substrain of *Saccharomyces cerevisiae,* has an optimal growth in temperature of 37 °C and survives passage through all levels of the GI tract [10]. It was subsequently used in France for the treatment of diarrhea in the beginning of 1950 [9, 12]. *Saccharomyces boulardii* has a direct antagonistic effect on many pathogens. Its efficacy is attributed to a direct inhibitory effect on the growth of pathogenic strains, an anti-secretory effect by specifically binding toxins to intestinal receptors and a trophic effect on enterocytes with stimulation of enzymatic activity and nonspecific and anti-infectious mechanisms such as anti-inflammatory activity [14]. *Saccharomyces boulardii* secretes a protease which has been shown to neutralize certain bacterial toxins. It is also able to stimulate an immune response in the intestinal mucosa. It has a trophic effect by enhancing the metabolic function of the mucosa [9, 15]. *Saccharomyces boulardii* releases polyamines which result in an increased secretion of brush border disaccharidases and enzymes (such as lactase, sucrase, maltase and aminopeptidase) [14]. The increased secretion of polyamines enhances maturation of enterocytes. Polyamines increase the glucose carrier activity on the membrane of enterocytes which is essential to achieve maximal glucose absorption [14]. This study was performed in Kashan, Iran, to determine the effect of *S. boulardii* on the clinical course of acute watery diarrhea in children.

Subjects and methods

The children aged 6 months to 6 years with acute watery diarrhea admitted in pediatric clinic in Kashan (Iran) in 2012 were included in this randomized controlled clinical trial. Exclusive criteria were high fever ($T > 38.5$ °C), severe dehydration, bloody diarrhea, severe malnutrition, using of antibiotics, anti-diarrheal or antifungal drugs and patients with more than one complain. Parents received detailed information about the study, and those who agreed to participate signed an informed consent. Patients were alternately assigned to receive the probiotic (*S. boulardii*) plus ORS or placebo plus ORS. Two hundred patients were included in this trial and divided into two groups: A total of 100 patients were treated with *S. boulardii* that were prepared by Ardegpharm-GmbH, 250 mg once daily in addition to ORS (case group), and 100 patients were given placebo in addition to ORS (control group). Placebo and probiotic products have similar color and taste. They were treated for 5 days. The ORS was administered by WHO protocol for management of diarrhea. In the first visit on admission data about full clinical history, physical examination, nutritional status, dehydration, fever, oral tolerance and stool characteristics were recorded. The duration of diarrhea, consistency and frequency of stool were recorded by asking the mothers of the children every day during active treatment phase (5 days). Diarrhea was defined as the passing of three or more loose or watery stool for a day. Diarrhea was considered to have stopped when the child passed less than three stools per day or stool with solid consistency. Data analysis was performed by using the SPSS 16, and parametric statistical tests (*t* test and Chi-square) were employed to compare the two groups.

Results

Kolmogrove–Smirnov test showed that data had normally distributed; therefore, parametric statistical tests were employed to compare the two groups.

Table 1 presents the demographic characteristics of the children according to the treatment strategy and shows that the proportion of the two groups with regard to gender was not significantly different ($P = 0.56$).

Table 2 presents the mean value of age for both treatment strategies and shows that there is no significantly difference between the two groups ($P = 0.17$).

Table 3 presents duration of diarrhea according to the treatment strategy and shows that is significantly less for the case group than for the control group (3.4 vs 5.5 days) ($P = 0.001$).

Table 4 presents the stool frequency of two groups during the treatment. On day 1 of treatment, the defecation frequency in two groups was similar (8.4 in the case and 8.1 in the control group) ($P = 0.47$). On day 2, it was 6.5 in the case group and 7.2 in the control group that there was no significant difference between two groups ($P = 0.07$). On day 3, stool frequency was 3.2 in the case group and 5.3

Table 1 Demographic characteristics of the patients according to the treatment strategy

Groups	Frequency	Gender	
		Girl	Boy
Case	100	40	60
Control	100	44	56
Total	200	84	116
P value = 0.56			

Table 2 Comparing the mean of age in treatment strategy

Groups	Frequency	Age (month)	SD
Case	100	16.2	13.18
Control	100	18.2	14.76
Total	200	17.2	14.04
P value = 0.17			

Table 3 Duration of diarrhea in both groups

Groups	Frequency	Mean (days)	SD
Case	100	3.4	1.3
Control	100	5.5	2.1
P value = 0.001			

in the control group, and there was a significant difference between two groups ($P = 0.001$). On day 4, it was 2.1 for the case group and 4.1 for the control group; that two groups were different significantly ($P = 0.001$). On day 5, stool frequency was significantly less for the case group than for the control group (1.5 vs 3.2) ($P = 0.001$).

This table shows that the stool frequency was a significant reduction in the case group as compared to the control group from the third day of treatment.

Discussion

This study aimed to investigate the effect of a yeast probiotic (*S. boulardii*) in the treatment of acute gastroenteritis, and the results showed that the use of *S. boulardii* can reduce the duration of diarrhea (3.4 days in the case group versus 5.5 days in the control group). In one study that conducted by Grandy in children 1–23 months of age, hospitalized for acute diarrhea in Bolivia was seen that total duration of diarrhea was significantly shorter in children receiving *S boulardii,* and results show that *S. boulardii* diminished the time of diarrhea by 31.4 % and shortened time with fever by 73 %. The results of our study about the duration of diarrhea are consistent with these results [1]. In other study, Canani evaluate the efficacy of probiotics in 571 children aged 3–36 months with acute diarrhea in Italy [4]. Median duration of diarrhea was significantly shorter in children who received probiotics (78.5 h) than who received oral rehydration solution alone (115.0 h). The results of our study are consistent with these results [4]. In another study that performed by Htwe in 100 hospitalized children 3 months to 10 years in Belgium, 50 were treated with *S. boulardii* in addition to oral rehydration solution (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 in the control group [14]. The results of our study are consistent with these results; of course in our study, the probiotic was administered once daily but in above study twice daily. In another study by Billoo in Karachi, Pakistan, 100 children from 2 months to 12 years of age with acute diarrhea were randomized in *S. boulardii* group (treated with ORS, nutritional support and *S. boulardii*, 250 mg bid) and in control group (treated with ORS and nutritional support only). The duration of diarrhea was 3.6 day in *S. boulardii* group, whereas it was 4.8 day in control group. Therefore, this study confirms that the *S. boulardii* significantly reduces the frequency and duration of acute diarrhea [9]. Our results are consistent with the results of the above study. In the present study, defecation frequency in the first and second days of treatment does not show a significant difference between two groups ($P = 0.47$). Defecation frequency in the third, fourth and fifth day of treatment shows a significant difference between two groups. The results of this study indicate that the use of *S. boulardii* in the treatment of diarrhea can significantly reduce the stool frequency from the third day onwards.

In the Canani study was seen one day after the first probiotic administration, the daily number of stools was significantly lower in children who received probiotics [4]. The results of our study are consistent with these results. In this study, efficacy of *S. boulardii* perceived after the first day, but in our study was seen on the third day. In the

Table 4 Stool frequency during the treatment in both groups

Day of treatment	Groups						Significance (P value)
	Case			Control			
	Frequency	Mean	SD	Frequency	Mean	SD	
Day 1	100	8.4	2.7	100	8.1	3.2	0.47
Day 2	100	6.5	1.8	100	7.2	3.5	0.07
Day 3	100	3.2	1.3	100	5.3	1.62	0.001
Day 4	100	2.1	0.65	100	4.1	1.45	0.001
Day 5	100	1.5	0.73	100	3.2	1.04	0.001

Billoo study, stool frequency by day 3 was 2.7 in *S. boulardii* group and 4.2 in control group, and by day 6 it was 1.6 in *S. boulardii* group versus 3.3 in control group. These results showed that the *S. boulardii* significantly reduces the frequency of acute diarrhea [9] that was similar to our study. In another study that performed by Guillot in Havana, Cuba, 40 babies aged 6–36 months with chronic diarrhea were studied. The study confirms the beneficial effect of *S. boulardii* in chronic diarrhea caused by a post-gastroenteritis syndrome, especially when it is due to giardiasis. Reduction in stools frequency was significantly lower in children who received probiotics [12].

In the study by Htwe was seen stools had a normal consistency on day 3 in 76 % of patients in the *S. boulardii* group compared with only 24 % in the control group. On day 2, 54 % had less than three stools in the *S. boulardii* group compared with only 30 % in the control group. *Saccharomyces boulardii* shortens the duration of diarrhea and normalizes stool consistency and frequency [14]. The results of our study are consistent with these results.

Conclusion

The results of our study and other similar studies about administration of the yeast probiotic proved that *S. boulardii* can substantially reduce the severity and duration of diarrhea in children. According to the efficacy of the bacterial probiotics on diarrhea recommended further studies to be performed to compare the effects of bacterial and yeast probiotics in children with gastroenteritis.

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Compliance with ethical standards

Conflict of interest The authors declared that they have no competing interests.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments.

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