International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 09, Issue 05, May 2024,
https://doi.org/10.23958/ijirms/vol09-i05/1895

Original article

An Interventional Study to Measure the Role of Probiotics in Treating Diarrhea in Sample of Children in Fallujah City, Iraq

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Received 10 April 2024; Accepted 12 May 2024; Published 14 May 2024

Abstract

Background: Diarrhea, a life-threatening condition in children under two years, is largely controllable with probiotics, which colonize the bowel, reducing the severity and duration of acute diarrhea. The study aims to evaluate the effectiveness and role of probiotics in treating diarrhea in children under two years old. ***Methods:*** The study is an open-label, nonblinded randomized controlled trial that followed 60 patients in Fallujah city. Patients were divided into two groups, one receiving probiotics and the other not. Treatments included oral rehydration solution, lactose-free formula, and zinc supplementation. Probiotics used were yeast-derived "saccharomyces boulardii". The confidence level was 95%. ***Results:*** The average age of the children was 10.8 ± 5.8 months, 50% of them were males and the majority 83.3% were on milk formula. The duration of the diarrhea among the included children were significantly shorter among the group who has been given probiotics by about one day compared to other group, with adjustment to their age [B= -0.744, (95% CI: -1.455 to -0.033)]. The magnitude of probiotic treatment effect found to shorten the duration of the diarrhea by 50%. ***Conclusions:*** The study indicates that co-administration of probiotics with standard rehydration therapy reduces diarrhea duration by a mean of 1 day in children under 2 years old, and by 50%.

Keywords: ***Under two years children, Diarrhea, Probiotics.***

Introduction

Diarrhea is a life-threatening condition especially in children under two years; about 80% of deaths due to diarrhea occur in the first two years of life [1]. Deaths due to diarrhea in under five children fell gradually from 0.08 % in 2003 to 0.05 % in 2017 in Iraq [2]. In India about 10% of infants and 14% of under five children die due to diarrhea. Incidence of gastroenteritis is highest in the first two years of life and it represents a public health problem worldwide and remains the second leading cause of death among children under five globally [3]. Dehydration, hypokalemia and acidosis are the main life- threatening complications, Low osmolality oral rehydration solution (ORS) and zinc are the two effective interventions introduced in the last two decades for diarrhea management. However, its use neither shortens the duration of the illness nor reduces the stool loss. Several trials on probiotics, as an adjuvant to oral rehydration therapy have been conducted in the recent years using different probiotic strains with variable outcome, found to reduce the duration of illness [3,4].

Probiotics are defined as microorganisms that when administered in adequate amounts denote a health benefit on the human health. Probiotics colonize the bowel effective in reducing the severity and duration of acute diarrhea in children, most commonly; Lactobacillus rhamnosus L plantarum, several strains of bifidobacteria, Enterococcus faecium, the yeast Saccharomyces boulardii, and preparations containing a mix of strains. A study in Italy exposed probiotics were the most commonly prescribed treatment for children with diarrhea [5,6]. Saccharomyces boulardii, a non- pathogenic yeast has been proven to be efficacious in many studies, as a study of Sinchana Bhat, et.al, showed Saccharomyces boulardii is effective in reducing the duration of diarrhea and hospital stay in under five children with acute gastroenteritis in compared to group have been given ORS and zinc and another group have been given Bacillus clausii [7,8].

A randomized Controlled Trial of Gladys Villarruel, et.al, revealed S. boulardii as an adjuvant to ORS in ambulatory care in children less than two years old with mild or moderate acute diarrhea decreased the duration of diarrhea, accelerated recovery and reduced the risk of prolonged diarrhea in compared to placebo group [9]. A study of Mayuresh Kiran, et.al, exhibited Saccharomyces boulardii is safe and efficacious in the treatment of diarrhea in Indian children and it decrease the course of diarrhea [10].

The study aims to compare the effect or the role of using probiotics in the treatment of diarrhea in children under two years of age.

Patients and methods

The current study is an open label nonblinded randomized controlled trial which followed 60 patients by follow-up visits to primary health care centers, Fallujah city during the period from April 2023 through October.

Inclusion criteria

children aged 24 months or younger with acute diarrhea (three or more watery or loose stools per day) with mild to moderate dehydration which does not need intravenous fluid or hospital admission [11]. The parents or the guardians of each child who met the inclusion criteria has been approached for clarifying the aims and interventions of the study to sign the informed consent for inclusion in the study, otherwise we excluded them.

Exclusion criteria

Systemic infection requiring antibiotic; or bloody diarrhea

The intervention

The patients were randomly divided into two groups (The parents or guardian of every eligible patient were interviewed and asked to give their consent for participation in the study with every other one assigned to different group); one group received probiotics and the other not; the two groups were matched regarding the other treatment in form of oral rehydration solution, lactose free formula for formula fed babies, zinc supplementation 10-20 mg daily for 10-14 days. The probiotics used are yeast derived probiotics called *saccharomyces boulardii*.

Sample size

The sample was convenient, every other patient was assigned to receive probiotics. Sixty patients whom completed the follow up visit and fulfilled the inclusion criteria were included.

Outcomes

The outcome variable was the duration of the diarrhea, and the fellow up for each child in both groups extended on daily bases for seven days after giving the probiotics to group 1.

Ethical considerations: The ethical and scientific approvals were signed from the committees in the Arab board for Health Specialties, Al-Anbar health directorates and the administrative units in the included Primary health centers in Al Fallujah city, before the beginning of data collection. In addition, an informed consent was formed and clearly explained for the children's parents or guardians to be signed before the inclusion in the study.

The data collected using a preformed questionnaire including children's age by month, sex, feeding status (Breast feeding or formula) and weather they were in group 1 (received probiotics) or group 2 (not received probiotics) as well as the duration of the diarrhea which followed by follow up visits to primary health care centers

Statistical analysis

The data were gathered from the children then entered, cleaned and analyzed using Statistical Packages for Social Sciences (SPSS ver.26). The categorical variables presented by frequencies and percentages and the association between the groups and sex or feeding type were tested by Pearson's chi-square test of dependence. The numerical variables presented by mean and standard deviation and the difference between the study groups was tested using Independent t-test, then the variables with p-value <0.1 fitted into a linear regression model to determine the predictors of the duration of the diarrhea among the study groups. The confidence level was 95%. The effect size of the trial was calculated according to the formula shown below [12].

$$\text{Effect size} = \frac{mean\ group\ 1 - mean\ group\ 2}{Standard\ deviation}$$

Results

The current study included 60 children under two years of age with acute diarrhea, the overall average age of the children was 10.8 ± 5.8 months, 50% of them were males and the majority 83.3% were on milk formula while 16.7% were on exclusive breast feeding.

The patients were divided into two equal groups, one group received the probiotics. There was no significant difference between the two groups regarding age, sex or feeding. Table 1

Table 1: Age, sex and feeding type of the included children

Variables	Probiotics		Total (n=60)	*P*-value
	Received (n=30)	Not received (n=30)		
	Mean ± Sd	Mean ± Sd	Mean ± Sd	
Age (months)	9.4 ± 6	12.1 ± 5.4	10.8 ± 5.8	0.067
Sex	**No. (%)**	**No. (%)**	**No. (%)**	
Male	13 (43.3)	17 (56.7)	30 (50)	0.302
Female	17 (56.7)	13 (43.3)	30 (50)	
Feeding				
Breast feeding	6 (20)	4 (13.3)	10 (16.7)	0.488
Formula	24 (80)	26 (86.7)	50 (83.3)	

Sd: standard deviation

The overall duration of the diarrhea among the children was 3.1 ± 1.4 days. The duration of diarrhea in males was longer than females (3.2 ± 1.4 vs. 2.9 ± 1.3 days, p=0.332), it was also longer among children fed by formula compared to breastfeeding children (3.1 ± 1.5 vs. 2.8 ± 0.8 days, p=0.332), however, these differences failed to reach significant level.

The effect of probiotics on the duration of diarrhea also compared according to the feeding of the included patients and the results showed that; the duration of diarrhea was longer among those who did not receive the probiotics in breastfeeding babies 3.0 ± 0.8 days with no significant difference (p = 0.548) with those received the probiotics 2.7 ± 0.8 days. Similarly, there was no significant difference in diarrhea duration among babies on formula according to receiving probiotics (Not received: 3.7 ± 1.5 vs. received: 2.7 ± 1.3 days, p=0.052). Table 2.

Table 2: Duration of diarrhea according to sex and feeding of the included children

Variables	Duration of diarrhea (days)	*P*-value
	Mean ± Sd	
Sex		
Male	3.2 ± 1.4	0.333
Female	2.9 ± 1.3	
Feeding		
Breast feeding	2.8 ± 0.8	0.332
Formula	3.1 ± 1.5	
Breastfeeding		
Probiotic received	2.7 ± 0.8	0.548
Probiotic not received	3 ± 0.8	
Formula feeding		
Probiotic received	2.7 ± 1.3	0.052
Probiotic not received	3.5 ± 1.5	

Sd: standard deviation

On the other hand, the duration of diarrhea was significantly shorter among the children who received probiotics, compared to those who did not (2.7 vs. 3.4 days, P= 0.036) Figure 1. The magnitude of treatment effect of the use of probiotics found to shorten the duration of the diarrhea by 50%.

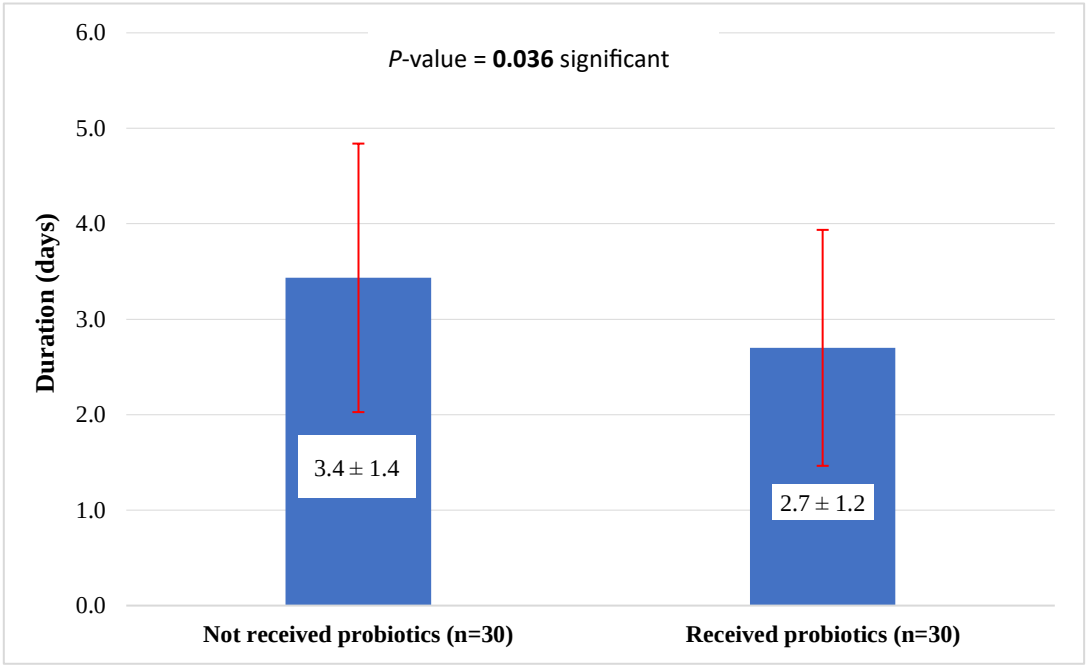

Figure 1: Comparison of average duration of diarrhea among the included children according to giving probiotics.

The duration of the diarrhea among the included children were significantly shorter among the group who has been given probiotics by about one day compared to other group, with adjustment to their age [B= -0.744, (95% CI: -1.455 to -0.033)]. Table 3

Table 3: Linear regression model for prediction of the duration of diarrhea according to its determinants

Variables	Coefficients of regression B	P-value	95.0% Confidence Interval for B	
			Lower Bound	Upper Bound
(Constant)	3.48	<0.001*	2.585	4.375
Age (months)	-0.004	0.902	-0.066	0.058
Probiotics	-0.744	0.041*	-1.455	-0.033
*Dependent Variable: Duration (days), *Significant at 0.05 level*				

Figure 2 illustrates the difference between the two groups according to the use of probiotics. It shows the number of the children that still have diarrhea each day after starting the treatment.

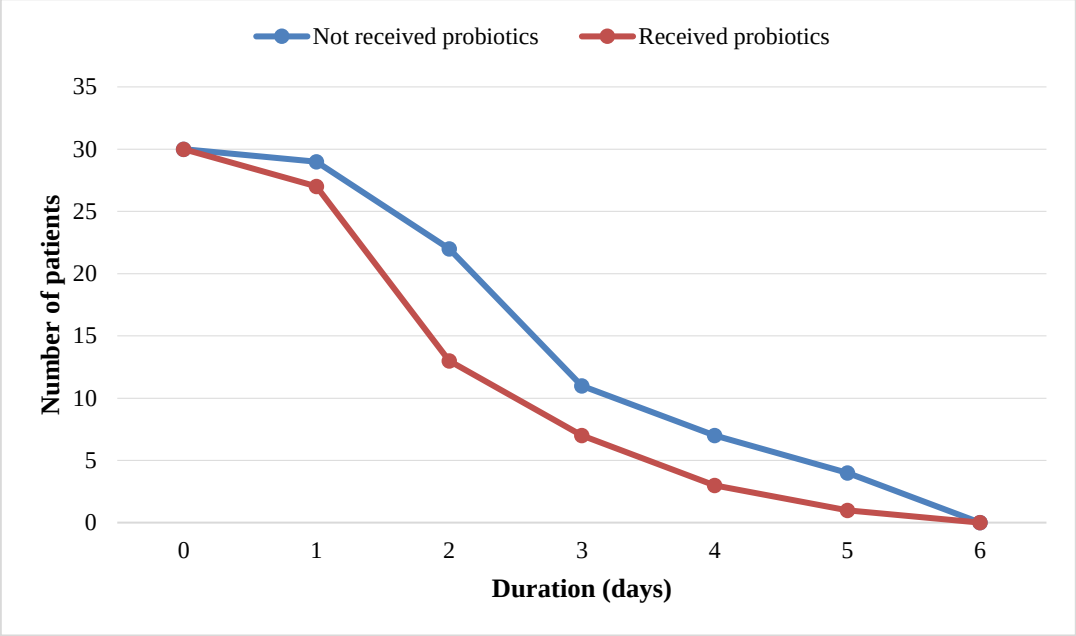

Figure 2 The number of patients in each study group across the duration of the treatment

Discussion

Diarrhea is still a major cause of childhood morbidity. It is also a source of anxiety to families of affected children and represents a heavy economic burden for families and for society as a whole [13,14]. Probiotics have progressively gained incredibility for the treatment of diarrhea [15-17]. However, micro-organisms purported to have probiotic properties are considered to be food additives rather than drugs [18].

In the present study, despite the immense benefits of breast feeding, it was not found to be a common practice, most of the included children 83.3% were on formula feeding while only 16.7% were on exclusive breast feeding. This result was in line with other studies, in Saudi Arabia, Shati et al, 2020 showed that only 15.9% of the children were exclusively breastfed [19] and in Uganda, Otim et al ,2022 showed that only 10% of children were on exclusive breastfeeding [20].

The primary outcome measure in the current study was the duration of diarrhea. The overall duration of diarrhea in children less than 2 years in this study was 3.1 days, in children who received probiotics the duration of diarrhea was significantly shorter (2.7 days) in comparison to those who didn't receive probiotics (3.4 days). This was in line with Aggarwal et al study that showed that the mean duration of diarrhea was 2.5 days in those who used probiotics and 3.25 days in those who didn't [21] and Williams, 2010 study that found the mean duration of diarrhea in those who used probiotics was 2.9 days compared to 3.4 days in those who didn't[22].

In the present study, the magnitude of treatment effect of the use of probiotics was found to shorten the duration of diarrhea by 50%. This result was in line with Sazawal et al,2006 study that reported that probiotics reduced the duration of diarrhea by 52% [23]. Canani et al, 2007 study also reported a significant reduction in the duration of diarrhea in children receiving probiotics with an effect size of 39.4% [5].

The duration of diarrhea was longer in formula fed children compared to breastfed children although this difference failed to reach statistical significance in the current study, shorter duration of diarrhea in breast fed children had been reported in previous studies Lamberti LM et al, 2011 [24] and Rouw et al, 2018 [25].

In the current study no statistically significant difference in duration of diarrhea was found between breast fed children who received probiotics and breastfed children who didn't. This was in parallel with previous literatures that showed that exclusively breastfed children are already getting probiotics from mom's milk naturally and may not benefit from probiotics [26,27].

However, Rinne M et al, 2005 suggested that the use of probiotic therapy in exclusive breastfed children exert synergistic effects and may thereby improve the immune function [28].

In the present study, in formula fed children the duration of diarrhea was shorter in those who received probiotics compared to those who didn't (2.7 days compared to 3.5 days respectively), yet this difference failed to reach a statistically significant level. Previous literatures had reported shorter duration of diarrhea in formula fed children who received probiotics [29,30]. however, in ESPGHAN's nutrition committee analysis of formula fed infants no conclusive results were obtained due to considerable variability in the type and dose of probiotics used and supplementation periods[31].

After age adjustment, the duration of the diarrhea was significantly shorter among the group who has been given probiotics by about one day compared to other group, this was in line with Thibault et al, 2004 and Cimperman et al ,2011 as they reported shorter duration of diarrhea by 1 day in children and adults who used probiotics [32,33] Williams,2010 study also showed that the use of probiotics decrease the duration of diarrhea by 0.7 days [22].

Conclusion

The current study suggests that coadministration of probiotics (saccharomyces boulardii) with standard rehydration therapy reduces the duration of diarrhea by a by mean of 1 day in children less than 2 years of age. The magnitude of treatment effect of the use of probiotics was found to shorten the duration of diarrhea by 50% in children under 2 years of age.

Recommendation

Probiotics can be considered as a reliable add on supplements for treating diarrhea in children, as the use of prebiotics had led to some encouraging results concerning duration of diarrhea in children.

Further studies are needed to prove probiotics safety, effectiveness, dosage, and supplementation periods to broaden their coadministration with standard rehydration therapy for gastroenteritis in children.

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