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### Effect of probiotic treatment on acute diarrhea in childhood

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#### ABSTRACT

Probiotics are non-pathogenic live bacteria, grow in the intestines and regulate intestinal micro flora. The present study aimed to investigate the effects of probiotic treatment on acute childhood diarrhea. Through a randomized clinical trial, 80 children classified into two equal groups were recruited. Participants aged between 6 months to 5 years with non-bacterial gastroenteritis admitted to the pediatric wards in Sanandaj city, western Iran. The first and second groups received IV therapy plus probiotic yogurt and only IV therapy, respectively. Of 80 children, 52.5% were female. There were no significant differences before intervention in terms of age, gender, nutrition and severity of diarrhea. Severity of diarrhea was altered by 95% and 27.5% ( $p=0.0001$ ), and mean ( $\pm$ SD) hospitalization days were  $2.42 \pm 0.55$  and  $4.47 \pm 1.47$  in the first and second groups, respectively. The frequency of hospitalization days due to acute diarrhea, were  $2.42 \pm 0.55$  and  $4.47 \pm 1.47$  in the first and second groups, respectively. Consumption of probiotic yogurt reduces duration, severity and frequency of acute diarrhea in hospitalized children.

#### 1. Introduction

Diarrheal diseases are in charge for 1.8 million deaths (18%) amongst children annually. The World Health Organization (WHO) has estimated that annually over 5.2 million episodes of diarrhea and 700 million deaths due to diarrhea in children under 5 years occurs in developing countries. Although the overall mortality rate for children is declining, but the overall incidence of diarrhea has not changed (1). Rotaviruses are the most common cause of infectious diarrhea in childhood across the world.

Nowadays, treatment of diarrhea in children is limited to either symptomatic or supportive cares. These include oral fluid therapy, nutritional therapy for children at home and IV therapy in the hospital. Antibiotic therapy is not useful in 85-90% due to unknown or viral sources (2).

Probiotics are non-pathogenic live bacteria, grow in the intestines. Probiotics are often belonged to a large group of bacteria living harmlessly in the human intestine and regulate intestinal micro flora (3). Metabolic activities of the microorganisms have beneficial effects for the host as the intestinal flora has already shown a protective role against various diseases (4).

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Production of inhibitory compounds, competition for binding sites and nutrients, eliminating toxins receptors, strengthening the immune system and secretion, production and synthesis of short-chain fatty acid, lactic acid and bacteriocin are the main protection mechanisms of probiotics against gastrointestinal disorders. Probiotics are useful for maintaining the constancy of the intestine, reducing the effects of gastrointestinal diseases such as antibiotic-associated diarrhea, inflammatory bowel disease, childhood diarrhea, traveler's diarrhea, lactose intolerance, *H. pylori* infection, irritable bowel syndrome and intestinal disease caused by *Clostridium difficile* (5).

Probiotics have also some rare adverse effects and drug interactions (6,7). Consumption of probiotics in healthy individuals does not increase risk of bacterial infections. The risk even in patients with immunodeficiency is very low (8). Probiotics may also prevent antibiotic-associated diarrhea and acute diarrhea (9), and for treatment of acute diarrhea (4,10,11). However, there are some controversial results (12).

Children with diarrhea in developing countries including Iran are facing with dehydration, complications and psychological consequences due to hospitalization. The present study aimed to investigate the effects of probiotics consumption to decrease severity and duration of diarrhea in children aged 6 months to 5 years.

## 2. Materials and Methods

### 2.1. Sample collection

Through a randomized clinical trial in 2013, overall 80 children with nonbacterial gastroenteritis referred to the pediatric ward of Be'sat Hospital, Sanandaj city, Kurdistan province, western Iran were recruited. Inclusion criteria were age 6 months to 5 years, acute non-bloody nonbacterial diarrhea and moderate dehydration for less than 3 days. Children with antibiotic therapy, severe vomiting, seizure disorders, pneumonia, septicemia, malnutrition, immune deficiency, presence of inflammatory cells stool and shock were excluded from the study. Since in the previous studies, probiotic supplements have not been accepted by children; therefore, probiotic yogurt was used in the present study.

Through a randomized clinical trial, 80 children classified into two equal groups and aged between 6 months to 5 years with non-bacterial gastroenteritis who were admitted to the pediatric ward of Be'sat Hospital in Sanandaj city western Iran were recruited. The first and second groups were received IV therapy plus probiotic yogurt and only IV therapy, respectively. After obtaining a written consent from parents, a checklist including demographics, medical history, duration of diarrhea and hospitalization, weight gain, frequency and severity of diarrhea as well as feeding and treatment types was completed. Children were examined by pediatricians looking for diarrhea severity and daily dehydration status.

The block foursome sampling method was used for group classifications. It was a double-blind study, the physician and the patients were not aware of treatment groups. Data were analyzed through SPSS v. 20 using McNemar's Chi-square, t-test and Fisher exact tests ( $\alpha=0.05$ ).

### 2.2. Intervention process

Probiotic package contains 7 species, *Lactobacillus* Casey, *Lactobacillus* Rhamnosus, *Streptococcus* Thermophilus, *Bifidobacterium* Breve, *Lactobacillus* Acidophilus, *Bifidobacterium* Infantis, *Lactobacillus* Bulgaricus of British pharmacy company PIL. A trained nurse was giving probiotics and yogurt twice a day for 2 days. The severity of diarrhea, frequency of diarrhea and dehydration status of children was assessed by a pediatrician daily.

The proposal of the present study was approved by the Ethics Committee at the Kurdistan University of Medical Sciences.

## 3. Results

Of 80 children, 52% were female (Table 1). Severity of diarrhea was altered in the intervention and control groups by 95% and 27.5% respectively ( $p=0.0001$ ). Mean hospitalization days were  $2.42 \pm 0.55$  and  $4.47 \pm 1.47$  in both groups respectively.

In the present study, there were no significant differences before intervention in terms of age, gender, nutrition and severity of diarrhea. Diarrhea was more frequent in control group than in intervention group. Severe diarrhea was not occurred in the intervention group ( $p=0.0001$ ). The frequency

**Table 1.** Clinical and demographic characteristics of intervention and controls

Characteristics	Intervention n (%)	Control n (%)	P value
Gender			
Male	18 (45)	21 (52.5)	0.52
Female	22 (55)	19 (47.5)	
Infant feeding			
Breastfeeding	26 (74)	23 (72)	0.82
Dry milk	9 (26)	9 (18)	
Frequency of diarrhea			
0	9 (22.5)	1 (2.5)	0.009
1	12 (30)	17 (42.5)	
2	13 (32.5)	8 (20)	
3 & more	6 (15)	14 (35)	
Severity of diarrhea			
Mild	39 (97.5)	4 (10)	0.0001
Moderate	1 (2.5)	29 (72.5)	
Severe	0 (0)	7 (17.5)	
change in severity of diarrhea			
Yes	38 (95)	11 (27.5)	0.0001
No	2 (5)	29 (72.5)	

**Table 2.** Comparison of continues characteristics in interventions and control groups

Variables	Groups*	Mean $\pm$ SD	P value
Age (month)	Intervention	17.85 $\pm$ 13.99	0.75
	Controls	19.85 $\pm$ 12.63	
Hospitalization (day)	Intervention	2.42 $\pm$ 0.55	< 0.001
	Controls	4.47 $\pm$ 1.47	
Weight gain(kg)	Intervention	227.50 $\pm$ 112.1	0.014
	Controls	123.75 $\pm$ 145	
Diarrhea frequency difference**	Intervention	6.33 $\pm$ 1.54	< 0.001
	Controls	4.65 $\pm$ 1.61	
Duration of diarrhea	Intervention	4.70 $\pm$ 0.69	< 0.001
	Controls	6.88 $\pm$ 1.40	

\*1. Probiotic + Yogurt, 2. Yogurt, 3. Control group

\*\* Admission to discharge days

of hospitalization days due to acute diarrhea, were  $2.42 \pm 0.55$  and  $4.47 \pm 1.47$  for the intervention and control groups (Table 2).

#### 4. Discussion

In this study severity of diarrhea was altered in the first and second groups by 95% and 27.5% respectively ( $p=0.0001$ ). Mean hospitalization days were  $2.42 \pm 0.55$  and  $4.47 \pm 1.47$  in both groups respectively. Severe diarrhea was not occurred in the intervention group ( $p=0.0001$ ).

Probiotic therapy is assumed to be based on the normal intestinal micro flora. Using probiotics is quite affordable via decreasing antibiotic resistance, increasing safety and inhibiting pathogens (5).

A recent study in Mashhad Northeast Iran using the same inclusion criteria and methodology, showed that the reduction rate of diarrhea frequency were 4.4 and 3.6 in probiotic and control groups which is consistent with the present study (4). Meanwhile, In Urmia city Northwest of Iran, frequency of diarrhea was 4.3 in children under 2 years receiving probiotic and 6.3 times in the control group (10).

Frequency of diarrhea amongst Indian children who received probiotics was lower than the control group, although the difference was not significant statistically (13). In the present study the severity of diarrhea was reduced after probiotic intervention. The severity of diarrhea in children who received probiotics was more quickly reduced than those treated by plain yogurt.

These reduction rates were 95% in probiotic group and 27.5% in control group ( $p= 0.0001$ ). In the Rosenfeld's study, this rate was reported to be 20% in the intervention group and loose stools after intervention was in probiotic group was less than one-third of control group (14). Shornikova and colleagues have also shown that the watery diarrhea was very low in probiotic intervention group compared to the control group (15).

The duration of hospitalization due to acute diarrhea, were  $2.42 \pm 0.55$  and  $4.47 \pm 1.47$  in the probiotic and control groups respectively indicating the influence of probiotic consumption to reduce the inpatient days. This finding is consistent with other studies that hospital stay for probiotic group was half than that of the control group. The

reduction of the hospital stay is important for the household economy and of psychological effects of hospitalization (4,14,16,17).

Children who received probiotics treatment, had weight gain more than other groups. Children's weight gain between admission and discharge were 227g, and 124g in probiotic and control groups ( $p=0.0001$ ). In Mashhad and Urmia studies, weight gain in children who received probiotics were more than control group which is consisted with the findings in the present study. There are different reports indicating that weight gain was more than the present study which may be due to conducting the study amongst older children (4,10).

Duration of diarrhea in children who received probiotics was  $4.7 \pm 0.7$  days, which was lower than the control group. In the Mashhad study, duration of diarrhea in probiotics group was less than the control group (4). Also in the Rosenfeld's study, duration of diarrhea were 3.4 days in probiotic and 5.4 days in control group (14). In a study, the corresponding duration was decreased by less than 3 days as reported by Szajewska and colleagues (16). A review study conducted by Guandalini and colleagues showed that using probiotics can reduce diarrhea for more than a day (18). A recent Finish study on children aged 6-36 months using lactobacillus router showed that the duration of diarrhea was reduced to 1.7 days (15). Similar results have been reported from India (17). An American meta-analysis showed that probiotics consumption was quite effective and safe in treatment of acute diarrhea (2). However, another systematic review showed lower effects for probiotics consumption (17).

Considering pathophysiology and mechanism of effect, many studies have shown that co-administration of rotavirus vaccine with lactobacilli safety, was associated with an increase in vaccine immunity. Oral probiotics had preventive and therapeutic effects on intestinal viruses due to lymphoid tissue irritation on virus and increased humoral immunity response (18). Lactobacilli are connected to peripheral blood CD4 and CD8 lymphocytes and are capable for binding to intestinal epithelial cells and activating macrophages (19).

## 5. Conclusion

In conclusion, consumption of probiotics yoghurts reduces the duration, severity and

frequency of diarrhea in hospitalized children with acute diarrhea.

## Conflict of Interests

Authors have no conflict of interest.

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