

Probiotics in the Treatment of Acute Diarrhea in Young Children

Hamid Reza Kianifar¹, Reza Farid²,
Hamid Ahanchian², Farahzad Jabbari²,
Toktam Moghiman², Armin Sistani³

Abstract

Background: Well-controlled clinical studies in the developed world have shown that probiotics can shorten the duration of acute non-bacterial diarrhea. We aimed to evaluate the efficacy of a probiotic consisting of a mixture of *Lactobacillus acidophilus* and *Bifidobacterium bifidum* in the treatment of young children with acute diarrhea in Mashad, Iran

Methods: Sixty-two hospital inpatients aged 6 to 36 months with acute non-bloody, non-bacterial diarrhea of a less than 2 days' duration and moderate dehydration were enrolled. Thirty-two were treated with probiotic powder three times daily for 5 days plus the routine oral rehydration solution (study group) and the other 30 were given a placebo plus oral rehydration solution (control group).

Results: Mean age at the time of admission was 14.5±7 months for the study group and 13.7±6 months for controls. The mean duration of diarrhea was 3.4 days in the study group and 4.5 days in controls ($P = 0.027$). Duration of hospital admission was 2.1±0.7 days in the probiotic group compared with 2.7±0.6 days in the control group ($P = 0.033$). Average weight gain was 425 ± 9 and 370 ± 85 g for the study and control groups, respectively. Average reduction in the frequency of diarrhea per day was 4.4 ± 1.5 times for the study group and 3.6 ± 1.3 times for the control group.

Conclusion: *Lactobacillus acidophilus* and *Bifidobacterium bifidum* shortened the duration of diarrhea and hospital stay, and normalized stool frequency. The use of probiotics might be recommended for treating acute diarrhea in young children.

Iran J Med Sci 2009; 34(3): 204-207.

Keywords • Acute diarrhea • probiotic • *Lactobacillus acidophilus* • *Bifidobacterium*

Introduction

The gastrointestinal tract of the human fetus is sterile, but is exposed to many different species of microorganisms after birth. In healthy individuals it houses more than 400 species of bacteria. Under certain circumstances such as antibiotic therapy, the balance of bacteria within the gastrointestinal tract is changed, which might result in a reduction in the amount of beneficial bacteria.¹

Probiotics are live non-pathogenic bacteria that are similar to beneficial microorganisms found in the human gut. They colonize the intestine and modify the intestinal microflora. Their

¹Departments of Pediatric Gastroenterology,

²Pediatric Allergy and Immunology,

³School of Pharmacy, Mashad University of Medical Sciences, Mashad, Iran.

Correspondence:

Hamid Ahanchian MD,
Department of Pediatric Allergy and Immunology, Ghaem Hospital,
Mashad University of Medical Sciences,
Mashad, Iran

Tel: +98 511 8012770

Fax: +98 511 8428014

Email: hamidahanchian@yahoo.com

Received: 5 January 2009

Revised: 3 May 2009

Accepted: 14 May 2009

metabolic activities have beneficial effects for the host.² They may be used to prevent and treat antibiotic-associated diarrhea and acute viral diarrhea. They may also be useful in relieving symptoms of irritable bowel syndrome, inflammatory diseases such as Crohn's disease, and in treating atopic dermatitis in children. Significant adverse effects are rare and there are no known interactions with other medications.^{3,4} The mechanisms of action of probiotics against gastrointestinal pathogens include modification of environmental conditions, competition for nutrients, producing antimicrobial metabolites, and modulation of immune defense mechanisms.⁵

Because well-controlled clinical studies in the developed world have shown that probiotics can shorten the duration of acute diarrhea, we aimed to evaluate the efficacy of a mixture of *Lactobacillus acidophilus* and *Bifidobacterium bifidum* in the treatment of acute non-bacterial diarrhea in young children in Mashad, northeastern Iran.

Patients and Methods

The present study was a randomized, double-blind, placebo-controlled trial that lasted 18 months from April 2006 through September 2007, covering two summer seasons. It took place at Sarvar Children's Hospital, Mashad, Iran. From a total of 145 children admitted to the hospital assessed for eligibility, 77 were excluded according to the exclusion criteria and 68 children aged 6 to 36 months with acute non-bloody, non-bacterial diarrhea of less than 2 days' duration and moderate dehydration were included in the study. The exclusion criteria were severe dehydration, antibiotic consumption, severe vomiting, convulsion, and inflammatory cells in stool samples.

The patients were randomly divided into two groups (case or control) by a random number table sequence. Children in the case group received a probiotic (Infloran, one billion *L. acidophilus* and one billion *B. bifidum*, Laboratorio Farmaceutico SIT S.r.l., Mede, Pavia, Italy) in the form of a powder reconstituted by parents with 5–10 ml of water and administered orally as a suspension. The probiotic was given three times daily for 5 days together with routine hospital management. Infants in the control group received a placebo (maltodextran) plus routine hospital management. The probiotic and placebo sachets were matched for size, shape, and volume of contents. The blinding process was performed by a pharmacist. During the study, physicians and nurses on the emergency ward who were involved in

the management and follow-up of the patients, as well as all parents, were blinded to the treatment protocol.

Hospital management for moderate dehydration caused by possible non-bacterial gastroenteritis was a combination of intravenous fluid therapy, oral rehydration solution, and mother's milk in breast-feeding infants, or complementary food according to the patients' age. Stool analyses were performed for all patients and complete blood count, electrolytes, blood urea nitrogen, and creatinine levels were measured for selected patients as needed. The patients' status on admission including weight, frequency of stools, hydration status, and duration of diarrhea were recorded with the help of a questionnaire. Patients were visited daily during hospital admission by a single physician and then followed up after discharge (daily calls by an investigator and weekly visits up to 2 weeks later by the same physician).

Two patients in the treatment group and four in the control group were excluded from the study because of poor adherence. The study protocol was approved by the local ethics committee of Mashad University of Medical Sciences. Written informed consent was obtained for each infant from his or her parent.

For an α value of 0.05 and a power level of 80%, the sample size was estimated as 30 patients in each group. The data were analyzed with SPSS software (standard version 11) and Student's *t* test was used to compare differences between the two groups. A *P* value <0.05 was considered statistically significant.

Results

Table 1 shows the baseline characteristics of the study and control groups. The duration of hospital admission was 2.1 ± 0.7 days and 2.7 ± 0.6 days for case and control children, respectively. The mean difference between the two groups was 0.6 day ($P = 0.033$). The mean duration of diarrhea was 3.4 ± 0.8 days in the probiotic group and 4.5 ± 0.8 days in the control group ($P = 0.027$). Average reduction in the daily frequency of diarrhea was 4.4 ± 1.5 times for the case group and 3.6 ± 1.3 times for the control group; the difference (0.8/day) was statistically significant ($P = 0.042$, table 2). The patients were followed up for two weeks and no persistent diarrhea, relapse, or side effects were seen in either group.

Discussion

Diarrheal illnesses are usually self-limited in the developed world; however, in developing

Table 1: Baseline characteristics on admission of children aged 6 to 36 months with diarrhea in the case and control groups

Characteristics	Case	Control	P value
Number	32	30	
Age (months)*	14.5±7	13.7±6	0.42
Male/Female	18/14	16/14	0.5
Weight (g)*	9450±745*	9360±690	0.62
Frequency of defecation (per day)*	9.2±1.5*	8.8±0.9	0.24
Duration of diarrhea (days)*	1.8±1.2*	1.65±0.8	0.36

* Mean ± SD

Table 2: Treatment response rate in children aged 6 to 36 months after receiving a probiotic (case group) or placebo (control group)

Variable	Case	Control	P value
Hospital stay (days) **	2.1±0.7	2.7±0.6	0.033
Duration of diarrhea (days) **	3.4± 0.8	4.5±0.8	0.027
Weight gain (g)**	425±9	370±8	0.014
Reduction in defecation frequency**	4.4±1.5	3.6±1.3	0.042

**Mean ± standard error

countries they may lead to significant malnutrition, morbidities, and sometimes even death.⁶ The importance of probiotic bacteria such as *Bifidobacterium* and *Lactobacillus* in maintaining the intestinal barrier function and also in modulating mucosal and systemic immune responses is becoming evident.⁷ Yet more research is needed for a better understanding of the role of probiotics in reducing morbidity, mortality, and the cost of this type of disease in developing countries.⁸ It is important to note that not all commercially available probiotic preparations are effective in children with acute diarrhea, and pediatricians should choose bacterial preparations based on available effectiveness data.^{7,9}

Some well-controlled clinical studies have shown that probiotics shorten the duration of acute diarrhea,^{1,10,11} whereas in other trials probiotics had no effect on duration.¹² These inconsistent results might be caused by differences in study populations, ethnic varieties, type of the probiotic, or differences in the dosage of the probiotic and duration of treatment. The present study showed that administration of *L. acidophilus* and *B. bifidum* for 5 days to children with acute non-bacterial diarrhea can decrease the duration and frequency of diarrhea as well as the hospital stay. We also detected better weight gain in the case group compared with the control group.

To the authors' knowledge, this is the first study on probiotics in children with gastroenteritis in Iran. Traditionally, foods such as yogurt are used for diarrhea management in Iran. A study conducted by Pashapour and Iou in 2005 found that yogurt could be beneficial in infants with diarrhea.¹³

Because of the small sample size and lack of data on the etiology of diarrhea (particularly

on the involvement of rotaviruses), we were not able to assess which type of diarrhea responded best to treatment with the probiotic. Although rare, bacteremia and fungemia have been reported as adverse effects of probiotic administration.^{14,15} None of our patients experienced these adverse effects.

Conclusion

We concluded that *Lactobacillus acidophilus* and *Bifidobacterium bifidum* may be effective in acute non-bacterial diarrheal infection in young children. Considering that probiotic consumption is not economically affordable for most families in Iran, the probiotic could be added to selected foods such as yogurt or oral rehydration solutions. This may make use of the probiotic cost-effective and thus more acceptable to the parents. Therefore, we recommend manufacturing a special yogurt which contains the same probiotic species.

Acknowledgment

This present study was supported by a grant from the Vice Chancellery for Research, Mashad University of Medical Sciences. We also wish to thank Dr. Birjandi, Shaghayegh Ameli, Mrs. Sabeti and Mrs. Tavakolian from the Emergency Ward of Sarvar Children's Hospital for their kind cooperation in collecting the data.

Conflict of Interest: None declared

References

- 1 Thomsen M. Probiotics Enhancing Health With Beneficial Bacteria. *Alternative & Complementary Therapies* 2006; 12: 14-20.

- 2 Weizman Z, Asli G, Alsheikh A. Effect of a Probiotic Infant Formula on Infections in Child Care Centers: Comparison of Two Probiotic Agents. *Pediatrics* 2005; 115: 5-9.
- 3 Kligler B, Cohn A. Probiotics. *Am Fam Physician* 2008; 78: 1073-8.
- 4 Gill H, Prasad J. Probiotics, immunomodulation, and health benefits. *Adv Exp Med Biol* 2008; 606: 423-54.
- 5 Sanz Y, Nadal I, Sánchez E. Probiotics as drugs against human gastrointestinal infections. *Recent Pat Antiinfect Drug Discov* 2007; 2: 148-56.
- 6 Huang JS, Bousvaros A, Lee JW, et al. Efficacy of probiotic use in acute diarrhea in children: a meta-analysis. *Dig Dis Sci* 2002; 47: 2625-34.
- 7 Madsen K. Probiotics in critically ill patients. *J Clin Gastroenterol* 2008; 42: S116-8.
- 8 Guandalini S. Probiotics for children: use in diarrhea. *Clin Gastroenterol* 2006; 40: 244-8.
- 9 Canani RB, Cirillo P, Terrin G, et al. Probiotics for treatment of acute diarrhoea in children: randomized clinical trial of five different preparations. *BMJ* 2007; 335: 340-5.
- 10 Htwe K, Yee KS, Tin M, Vandenplas Y. Effect of *Saccharomyces boulardii* in the treatment of acute watery diarrhea in Myanmar children: a randomized controlled study. *Am J Trop Med Hyg* 2008; 78: 214-6.
- 11 Henker J, Laass MW, Blokhin BM, et al. Probiotic *Escherichia coli* Nissle 1917 versus placebo for treating diarrhea of greater than 4 days duration in infants and toddlers. *Pediatr Infect Dis J* 2008; 27: 494-9.
- 12 Khanna V, Alam S, Malik A, Malik A. Efficacy of tyndalized *Lactobacillus acidophilus* in acute diarrhea. *Indian J Pediatr* 2005; 72: 935-8.
- 13 Pashapour N, Iou SG. Evaluation of yogurt effect on acute diarrhea in 6-24-month-old hospitalized infants. *Turk J Pediatr*. 2006; 48: 115-8.
- 14 Muñoz P, Bouza E, Cuenca-Estrella M, et al. *Saccharomyces cerevisiae* fungemia: an emerging infectious disease. *Clin Infect Dis* 2005; 40: 1625-34.
- 15 Sipsas NV, Zonios DI, Kordossis T. Safety of *Lactobacillus* strains used as probiotic agents. *Clin Infect Dis* 2002; 34: 1283-4.