Prevention of Antibiotic-Associated Diarrhea in Infants by Probiotics

PIPOP JIRAPINYO, M.D.*, NARUMON DENSUPSOONTORN, M.D.*,
NUCHNOI THAMONSIRI, B.Sc.*, RENU WONGARN, B.A.*

Abstract

Probiotics administration has been claimed to prevent antibiotic -associated diarrhea. The investigators thus conducted a double blind, placebo controlled study of providing probiotics to infants and children with severe bacterial infections and receiving broad spechum antibiotics.

The results of the study showed that the group receiving probiotics had fewer diarrheal episodes (37.5%) than the control group (80%), although the numbers were too small for statistical analysis. In conclusion, probiotics administration to patients receiving high doses of broad spectrum antibiotics may prevent the occurrence of antibiotic-associated diarrhea. A further study with a larger number is required.

Key word : Probiotics, Antibiotic-Associated Diarrhea

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Probiotics have become popular recently, especially in infants with gastrointestinal disease. The duration of diarrhea caused by Rota virus infection was shortened significantly when Lactobacilli were adjuncted in the therapy[1,2]. Their role in gastrointestinal disease is still not clear. However, it has been proposed that they could improve immune function in the gastrointestinal tract[3]. Also, they can prevent the growth of pathogenic bacteria in the GI tract[4]. Administration of high doses of broad spectrum antibiotics to infants is often followed by diarrheal disease a couple of days after administration. This is called antibiotic-associated diarrhea. The mechanism by which this occurs is unknown.

* Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

The authors hypothesize that antibiotics produce a decrease in the host flora so that the intestinal milieu allows the growth of contaminated pathogenic bacteria. so, the infant subsequently develops diarrhea after a short period of antibiotic administration. So far, only one study has shown that Lactobacillus GG can prevent antibiotic-induced diarrhea[5]. The present study, therefore, aimed to show that providing probiotics very early in the period of administration of high dose broad spectrum antibiotics can prevent diarrheal disease in these patients.

MATERIAL AND METHOD

Study Design

This was a double-blind randomized placebo-controlled trial. Patients were randomized into 2 groups following a randomization list. Group I, the study group was given the lyophilized preparation of *Lactobacillus acidophilus* and *Bifidobacterium infantis*(Infloran) at a dose of 1 capsule three times a day for 7 days, while the control group, Group II, received placebo capsules which contained a small amount of sugar and followed the same dosing schedule. The test drugs and the placebo had to be given to the patients within 24 hours of admission to the study and not later than 24 hours following antibiotic administration.

Subjects

In-patients diagnosed with either sepsis or meningitis whose ages ranged from 1 to 36 months and were receiving high doses of one or more than one broad spectrum antibiotics were recruited into the study after written informed consent was given by one of the parents.

Exclusion criteria

1. Presence of diarrhea before the study
2. Conditions where enteral feeding was contraindicated.
3. Patients in a moribund condition
4. Patients with either primary or secondary immunodeficiency

The study was approved by the Ethical Committee of Faculty of Medicine, Siriraj Hospital, Mahidol University.

Laboratory investigations and monitoring

The following laboratory investigations were performed: complete blood count, urine examination, hemoculture and serum electrolytes. Those who were diagnosed with meningitis underwent lumbar puncture and cerebrospinal fluid was sent for culture. The characteristics and frequency of stools were recorded. Clinical course of the patients was closely followed each day. Unexplained worsening of their clinical condition which might be due to Lactobacilli or Bifidobacterium sepsis was investigated and the investigators broke the code of that sample. If the sepsis was due to probiotics administration, the study was terminated.

RESULTS

A total of 18 patients were recruited into the study of whom 8 patients were in the study group and 10 patients were the control group. The characteristics of these patients are listed in Table 1. Most of the cases were diagnosed with meningitis. There was one case and 2 cases who were diagnosed with sepsis in Group I and Group II, respectively. All cases received high doses of broad spectrum antibiotics.

Table 2 shows the frequency of diarrheal diseases during treatment for the study group and the control group. There were 3 out of 8 cases in the study group (Group I), whereas there were 8 out of 10 cases in the control (Group II) who developed diarrheal diseases during the study. The investigators could recruit only 18 cases into the study as the test drug expired before. The numbers were small and not sufficient for statistical analysis. However, it appeared that the study group had fewer episodes of diarrhea than the control group. All diarrheal diseases in these patients were successfully controlled within a couple of days. There were no other complications found in these 2 groups of patients. All patients were finally discharged from the hospital after their primary disease was cured.

DISCUSSION

At present, there is a lack of well conducted clinical trials demonstrating any significant benefits of probiotics in humans. Probiotics and prebiotics modulate the composition of the human gut microbiota[6]. Administration of probiotics in acute diarrheal disease in infancy, especially to those who are infected with rota virus results in a shorter duration of diarrhea[7]. Children with rotavirus infection who received Bifidobacteria-supplemented formula may be protected against symptomatic rotavirus infection[8]. The mechanism of which is not yet clear. It is assumed that probiotics may improve the immune status of the gut milieu[3]. Also, the growth

Table 1. Characteristics of patients in the study group (Group I) and the control group (Group II).

Case	Age (month)	Sex	Diagnosis	Antibiotics treatment	Body weight (g)	Length (cm)
Group I						
1	4	F	Meningitis	Cefotaxime	6,780	61
2	3	M	Sepsis	Ampicillin + Gentamycin	3,000	50
3	36	F	Meningitis	Cefotaxime + Vancomycin	9,030	77
4	2	M	Meningitis	Ampicillin + Gentamycin	5,200	58
5	7	M	Meningitis	Cefotaxime + Cloxacillin	8,270	75
6	3	M	Meningitis	Cefotaxime + Ampicillin	4,550	52
7	10	M	Meningitis	Cefotaxime	9,660	84
8	4	F	Meningitis	Ceftriaxone	7,540	67
Group II						
9	3	M	Meningitis	Cefotaxime	4,750	57
10	8	M	Meningitis	Cefotaxime	9,180	75
11	24	F	Meningitis	Cefotaxime	9,750	93
12	6	M	Meningitis	Cefotaxime	4,200	54
13	3	F	Meningitis	Cefotaxime + Ampicillin	5,750	57
14	4	M	Meningitis	Cefotaxime	6,300	64
15	2	M	Meningitis	Cefotaxime	4,550	54
16	2	F	Sepsis	Cefotaxime	4,820	60
17	2	M	Sepsis	Cefotaxime	2,180	45
18	3	M	Meningitis	Cefotaxime	5,850	62

Table 2. Occurrence of antibiotic-associated diarrhea in study group (Group I) and control group (Group II).

Group	Number of cases who developed diarrhea	%	Date of start of diarrhea from initial treatment	Number of days of diarrhea
Group I	3 from 8	37.5	D3, D2, D2	4, 5, 4
Group II	8 from 10	80	D3, D1, D2, D3, D7, D5, D4, D6	4, 5, 3, 3, 2, 4, 7, 2

of probiotics may interfere with the growth of pathogenic bacteria[5]. There is little evidence from randomized, double-blind, placebo-controlled studies that bacterial probiotics have a significant beneficial action in preventing diarrhea from any cause. Our study has shown the effects of the probiotics given in preventing diarrhea from antibiotic-associated diarrhea. Although the number of cases in our study was not large, there appeared to be a difference between the 2 groups. Diarhea may complicate the recovery of patients who have sepsis or meningitis. Prevention or amelioration of diarrhea by probiotics is thought to be due to their effects on the immune system. Moreover, probiotics might prevent infection because they compete with pathogenic viruses or bacteria for binding sites on epithelial cells[9-11]. Probiotics might also inhibit the growth of pathogenic bacteria by producing bacteriocins such as nisin [12]. Thus, there is no harm in providing probiotics to small infants along with broad spectrum antibiotics when the patients are seriouly ill as a result of severe bacterial infection. In conclusion, the patients who were treated with high dose broad spectrum antibiotics and received probiotics seem to have fewer diarrheal episodes compared to the group who did not receive probiotics.

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การป้องกันการเกิดโรคอุจจาระร่วงจากยาปฏิชีวนะโดยโปรไบโอติคส์

พิภพ จิรภิญโญ, พ.บ., นฤมล เด่นทรัพย์สุนทร, พ.บ.*, นุชน้อย ธรรมนศิริ, วท.บ.*, เรณู วงษ์อาน, ศศ.บ.**

คณะผู้ทำการวิจัยได้ศึกษาการให้โปรไบโอติคส์ แก่ทารกที่มีการติดเชื้อแบคทีเรียอย่างรุนแรง และได้รับยาปฏิชีวนะ โดยรูปแบบ double-blind, placebo controlled โดยมีวัตถุประสงค์ว่า กลุ่มผู้ป่วยทารกที่ได้รับโปรไบโอติคส์จะมีอัตราการเกิดโรคอุจจาระร่วงน้อยกว่ากลุ่มควบคุม ผลการศึกษาพบว่ากลุ่มทารกที่ได้รับโปรไบโอติคส์จะมีอัตราเกิดจากอุจจาระร่วง (37.5%) น้อยกว่ากลุ่มควบคุม (80%) สรุปได้ว่าการให้โปรไบโอติคส์ แก่ผู้ป่วยทารกที่มีการติดเชื้อแบทีเรียอย่างรุนแรง และกำลังได้รับยาปฏิชีวนะอาจช่วยลดอุบัติการณ์โรคอุจจาระอันเนื่องจากยาปฏิชีวนะ

คำสำคัญ : โปรไบโอติคส์, โรคอุจจาระร่วงจากยาปฏิชีวนะ

พิภพ จิรภิญโญ, นฤมล เด่นทรัพย์สุนทร, นุชน้อย ธรรมนศิริ, เรณู วงษ์อาน
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* ภาควิชากุมารเวชศาสตร์, คณะแพทยศาสตร์ศิริราชพยาบาล, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10700