MANAGEMENT OF INFANT DIARRHEA WITH HIGH-LACTOSE PROBIOTIC-CONTAINING FORMULA

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Abstract. To study the influence of high-lactose probiotic-containing formula on the course of acute diarrhea, an experiment using a randomized controlled clinical trial with patients having acute diarrhea for 3 days was conducted. One hundred patients were allocated into two groups that were comparable for age, sex, and nutritional status. The test group was administered high-lactose *Bifidobacterium bifidum*-containing formula, while the control group had no high-lactose probiotic until the end of the experiment. The degree of subsequent diarrhea and recovery were monitored in both groups. The results for the test and control groups were analyzed and compared using the chi-square test and Fisher exact test with a significance level (α) of 0.05. The study results revealed that there was no significant difference between the test and control groups ($p>0.05$) as well as at positive clinical test (13%) and positive floating test (65%). However, the patients receiving probiotic-containing formula had significantly less frequency of stools, when compared with the control group ($p<0.05$).

INTRODUCTION

The use of low lactose and lactose-free milk is common in managing clinical diarrhea because lactose intolerance is common in diarrheal patients. Low lactose or lactose-free milk formula in diarrheal cases seems to have beneficial effects. On the other hand, lactose is an important nutrient because it is changed into galactose and glucose by lactase enzymes (Swallow *et al*, 2001). Using a high-lactose formula with diarrheal patients will normally prolong disease, but when a high-lactose formula is combined with a probiotic, it will improve lactose digestion. Probiotics are live anaerobic bacteria having lactase enzyme activity, since ß-galactosidase is released by destruction of the bacterial cell wall (de Vrese *et al*, 2001). According to this hypothesis, using high-lactose probiotic-containing formula will be beneficial in managing diarrheal cases. The objective of this study was to examine the influence of high-lactose probiotic-containing formula on the course of acute diarrhea.

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MATERIALS AND METHODS

Study design

This study used a random controlled clinical trial with patients having acute diarrhea for 3 days and was conducted at the Department of Child Heath, Soetomo Hospital, Surabaya. One hundred patients were allocated into two groups comparable for age, sex, and nutritional status. Excluded from the study were children with a history of high-lactose probiotic-containing formula use within 7 days before admission, acute gastroenteritis for more than 3 days before admission, patients with symptoms other than diarrhea (*eg* severe malnutrition, septicemia, CNS infections, bronchopneumonia and other severe infections). The high-lactose formula containing *Bifidobacterium bifidum* [dose 10^8 colony forming unit (cfu) per gram] was administered to the test group. The control group received no high-lactose probiotics until the end of the experiment. Stool cultures were obtained from all patients on the first day of admission. Both groups were monitored for their subsequent diarrheal course and recovery.

Specimens and analysis

The chi-square test or Fisher exact test were used to compare the subjects' characteristics (de-

hydration status, breastfeeding, stool culture and recovery state). The Student's *t* test was used to compare stool frequency and duration of diarrhea between the two groups, with a significance level (α) of 0.05.

Ethical considerations

The Ethics Committee of Dr Soetomo Hospital, Surabaya, gave approval for the study. The parents received verbal and written information about the study and were informed that there were no predictable risks to the patient, that blood sampling or other treatment could be associated with some discomfort, that all records were confidential, and that they could at any time withdraw from the study. Informed consent was obtained.

RESULTS

The age distributions for high-lactose probiotic and control groups is presented in Fig 1. There was no statistically significance difference in age distribution. The comparison of admission characteristics, result of stool cultures, and stool frequency per day of the study subjects and control group revealed no statistically significant difference (Tables 1, 2, 3). The use of high-lactose probiotic-containing formula showed improvement in the patients, such as stool frequency per day, duration of diarrhea and duration of hospitalization (Tables 3, 4, 5, 6).

DISCUSSION

Poor lactose digestion is the most common intestinal carbohydrate digestion disorder in humans. Although virtually all infants can digest milk sugar lactose, there is a slow decline in lactase activity in childhood. About 50% of African-American children are lactose maldigesters by 12 years of age and adults of most ethnic groups are lactose maldigesters. This condition worsens due to the reduction or loss of lactase activity in the intestinal brush border because of viral or bacterial infections. Ingestion of lactose by a person with lactose maldigestion may lead to abdominal bloating, flatulence, and may prolong diarrhea (Saltzman *et al*, 1999).

Normally, brush-border membrane maltase-glycoamylase-sucrase-isomaltase and lactase convert carbohydrate into glucose and lactose. Lactose will be changed to glucose and galactose which are taken into the absorptive cells by the sodium-dependent glucose transporter SGLT1 (Swallow *et al*, 2001). However, in diarrheal cases, undigested lactose in the large intestine serves as a fermentable substrate for bacterial flora

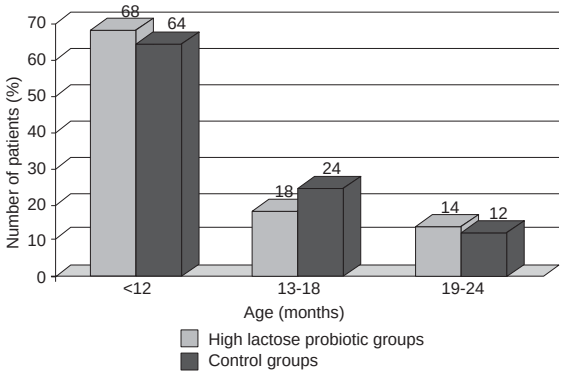

Fig 1–Age distribution for high-lactose probiotic and control groups. Statistical analysis found no significant difference in age distribution.

Table 1
Admission characteristics of the study subjects.

Characteristics	High-lactose probiotic group (n=50)	Control group (n=50)
Mean age (mo)[a]	11.5	11.7
Sex[b]		
Male	27(54%)	28(56%)
Female	23(46%)	22(44%)
Nutritional status[c]		
Underweight	18(36%)	20(40%)
Well-nourished	31(62%)	29(58%)
Overweight	1(2%)	1(2%)
Feeding[d]		
Breastfeeding	26(52%)	30(60%)
Non-breastfeeding	24(48%)	20(40%)
Mean duration of diarrhea (days) before admission[e]	1.9	2.1

[a]Student's *t* test; t = -0.127; df=98; p=0.899 (not significant); [b]Chi-square test; χ^2 =0.040; df=1; p=0.841 (not significant); [c]Chi-square test; χ^2 =0.172; df=2; p=0.841 (not significant); [d]Chi-square test; χ^2 =0.649; df=1; p=0.420 (not significant); [e]Student's *t* test; t = -0.1248; df=98; p=0.215 (not significant).

Table 2
Result of stool cultures of high-lactose probiotic, and control groups.

Results	High-lactose probiotic group (%)	Control (%)	Total (%)
Aerobic bacteria[a]			
Negative	29 (58)	29 (58)	58 (58)
E. coli	18 (36)	18 (36)	36 (36)
Klebsiella	2 (4)	1 (2)	3 (3)
Shigella flexneri	0 (0)	2 (4)	2 (2)
E. coli – Klebsiella	1 (2)	0 (0)	1 (1)
Anaerobic bacteria[b]			
Negative	37 (74)	33 (66)	70 (70)
Positive*	13 (26)	17 (34)	30 (30)
Rotavirus[c]			
Negative	24 (48)	21 (42)	45 (45)
Positive	26 (52)	29 (58)	55 (55)

[a]Chi-square; χ^2=3.333; df=4; p = 0.504 (not significant); [b]Chi-square; χ^2=0.762; df=1; p = 0.383 (not significant); [c]Chi-square; χ^2=0.364; df=1; p=0.546 (not significant); **Bifidobacterium*.

Table 3
Distribution of malabsorption.

Malabsorption test	High-lactose probiotic group (%)	Control group (%)	Total (%)
Clinitest[a]			
Negative	44 (88)	43 (86)	87 (87)
Positive	6 (12)	7 (14)	13 (13)
Floating test[b]			
Negative	19 (38)	16 (32)	35 (35)
Positive	31 (62)	34 (68)	65 (65)

[a]Chi-square; χ^2=0.088; df=1; p=0.766 (not significant); [b]Chi-square; χ^2=0.396; df=1; p=0.529 (not significant).

Table 4
Distribution of mean stool frequency per day.

Day	High-lactose probiotic group			Control group			t	df	p
	N	Mean	SD	N	Mean	SD			
0	50	9.62	4.12	50	9.84	4.04	-0.270	98	0.788[a]
1	50	5.78	3.64	50	8.14	3.26	-3.414	98	0.001[b]
2	50	3.46	2.42	50	6.22	3.05	-5.019	98	0.001[b]
3	24	2.96	1.37	50	4.06	2.84	-2.254	72	0.027[b]
4	8	2.50	0.76	29	3.52	2.23	-2.064	33	0.047[b]
5	1	2.00	-	17	3.00	2.09	-	-	-[c]
6	0	-	-	6	2.33	1.86	-	-	-[c]
7	0	-	-	1	2.00	-	-	-	-[c]

Student's *t* test; [a] = not significant; [b] = significant (p<0.005); [c] = not analyzed

Table 5
Duration of diarrhea for high-lactose probiotic and control groups.

Groups	N	Mean (days)	SD
High-lactose probiotic	50	1.1	1.0
Control	50	2.6	1.0

Student's *t* test; t=-7.78; df=98; p=0.001 (significant); The average duration of diarrhea was 1.1 days for the high-lactose probiotic group, compared with 2.6 days for the control group. Statistical analysis found a significant difference in the duration of diarrhea between the two groups ($p<0.005$).

Table 6
Duration of hospitalization for the high-lactose probiotic and control groups.

Groups	N	Mean (days)	SD
High-lactose probiotic	50	2.6	0.8
Control	50	4.0	1.1

Student's *t* test; t= -7.33; df=98; p=0.001 (significant).

and osmotically increases water flow into the lumen (de Vrese *et al*, 2001). For that reason, low lactose and lactose-free milk are commonly used in the clinical management of diarrhea and seem to have beneficial effects. On the other hand, lactose is very important for the myelinization of neural fiber, so that the use of low lactose or lactose-free milk formula with diarrhea cases with lactose maldigestion over a long period is not beneficial for the patient.

Using high lactose probiotic containing formula might give beneficial effect on management of diarrheal cases. This clinical experiment was thus undertaken to determine the influence of high-lactose probiotic-containing formula upon the management of diarrhea. The high lactose formula combined with probiotic has a beneficial effect because of the lactase activity of the probiotic (de Vrese *et al*, 2001). Lactose digestion may be improved if the ß-galactosidase of the bacteria is released by destruction of the bacterial cell wall (de Vrese *et al*, 2001).

After being given high-lactose probiotic-containing formula there was a significant improvement in the subjects of the study. Probiotics are microorganisms that have a favorable influence on the physiologic and pathological processes of the host by their effect on the intestinal flora, and may play a role in improving human health. One of the putative effects is modulation of the immune function, by stimulating the activity of splenic NK cells. Oral feeding with probiotics stimulated the production of Th1 cytokines, resulting in repressed production of IgE antibodies against antigens (Chin *et al*, 2000; Erickson and Hubbard, 2000; Matsuzaki and Chin, 2000). Yasui *et al* (1999) also reported that oral administration of *Bifidobacterium* activated the humoral immune system, augmented anti-rotavirus IgA production, and protected against rotavirus infection.

In conculsion, the administration of high-lactose *Bifidobacterium bifidum*-containing formula positively influences the rate of recovery in acute pediatric diarrhea.

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