

Probiotic treatment in children with lactose intolerance – An open labeled the one group pre-test post-test experimental study

Zainul Arifin, Aswitha D. Boediarso, Taralan Tambunan

ABSTRACT

Background Lactose intolerance is the most common disorder of intestinal carbohydrate digestion. Probiotic that contains the correct strain in appropriate amount can be used as an alternative dietary for lactose intolerance patients.

Objective This study was designed to describe the role of probiotic in relieving lactose intolerance symptoms in children consumed full-cream milk.

Methods This study was a clinical trial. Inclusion criteria was children aged 12-14 years old, had a good nutrition and health status, with positive breath hydrogen test (BHT) result and lactose intolerance symptom(s), and their parents gave consent. Forty-two children were included. All subjects consumed one glass (200 ml) of full-cream milk twice a day for 21 days and recorded intolerance symptoms. Probiotic was added from 8th to 21st day in their milk, and responses of treatment were evaluated by scoring system (based on borborigmic, flatulence, abdominal bloating, nausea and vomiting, abdominal pain, and diarrhea symptoms). At the end of study they were undergone second BHT examination.

Results There were decreasing mean score rates at 7th day (pre) 13.8 (SD 5.5) compared with 7.5 (SD 3.5) at 14th day (after) and was statistically significant ($P < 0.001$). Mean score rate at 7th day (pre) 13.8 (SD 5.5) compared with 21st day (after) was 0.119 (SD 0.55) and was statistically significant ($P < 0.001$). At the end of study, only 2 subjects showed clinical signs of lactose intolerance. Thirty-six subjects had normal BHT result at 21st day and was statistically significant ($P < 0.001$).

Conclusion Two weeks administration of probiotic could relieve lactose intolerance symptoms in children consumed full-cream milk [Paediatr Indones 2006;46:139-143].

Keywords: lactose intolerance, probiotic (*Lactobacillus acidophilus*, *Bifidobacterium longum*, and *Streptococcus faecium*), breath-hydrogen test (BHT).

Lactose is an important element in milk that acts as caloric resources, in breast milk, pure cow's milk even in the formula's milk.¹⁻³ Lactose is a disaccharide that can not directly be absorbed by the small intestine, but it has to be hydrolyzed into glucose and galactose.^{1,4} Lactose digestion into glucose and galactose was done by lactase enzyme that produced by the enterocyte cells at the brush border.⁵⁻⁷ Children that suffered from lactase deficiency have limitation in lactose absorption that can lead into lactose intolerance. Lactose intolerance may limit milk consumption that potentially caused children to suffer from nutrients deficiency such as calcium and protein that are needed for normal growth and development.⁸ There is a variety in prevalence of lactose intolerance among children. Higher prevalence (67-100%) is generally found in a population that is not used to consumed milk or dairy products after weaning.⁵

Probiotic in fermentation milk can reduce or diminish lactose intolerance condition because it can increase the activity of lactase enzyme at small intes-

From the Department of Child Health, Medical School, University of Indonesia, Jakarta, Indonesia.

Reprint requests to: Aswitha D. Boediarso, MD, Department of Child Health, Medical School, University of Indonesia, Jalan Salemba 6, Jakarta 10430, Indonesia. Telp.62-21-3907742; Fax 62-21-3907743.

tines and in the end of lactose process.⁸⁻¹¹ It is believed that milk consumption added with correct strain probiotic in appropriate amount can be used as an alternative dairy consumption for lactose intolerance patients. Thus they free to consume a milk product and as the result, nutrition's needs can be fulfilled.¹² The role of probiotic correcting lactose intolerance has not been conducted in Indonesia. In this study, we investigated the role of two weeks administration of probiotic in diminishing lactose intolerance symptoms in children who consumed full cream milk.

Methods

This study was a pre-experimental study with the one group pretest-posttest design in students who had proved to be lactose intolerance with BHT. This study was held at a junior highschool in Jakarta in July 2004.

Sixty-six students of 1st and 2nd grade were allocated using systematic sampling and underwent BHT screening. Forty-two 12-14 years old students were recruited with the inclusion criteria: had good nutrition and health status, had positive BHT, with self-reported lactose intolerance and had informed consent from his/her parents. Exclusion criteria included refusal to follow the

study, and had ever consumed probiotic product before. All subjects were given a glass (200 ml) of full cream milk (Dancow[®]) twice a day for 7 consecutive days and symptoms that reported was recorded. This period was regarded as pre-intervention duration. All subjects were then given 2 sachets of *Lacto-B*[®] probiotic (*Lactobacillus acidophilus*, *Bifidobacterium longum*, *Streptococcus faecium*) per glass of the full cream milk for the next 14 days. Symptoms appearing after ingestion of probiotic were also recorded. This was regarded as after intervention period. Re-examination of BHT was performed on the 21st day of observation.

Lactose intolerance symptoms were scored as follows:¹³ no symptoms=0, borborigmic=1, frequent flatulence=2, abdominal bloating=3, nausea and vomiting=4, abdominal pain=5, and diarrhea=6.

Results

From sixty-six cases allocated for study, only 42 children included in this study due to the limitation of the full cream milk available in this study.

Self-reported lactose intolerance symptoms in 42 children who had already given full cream milk are shown results in (Figure 1). All the clinical symp-

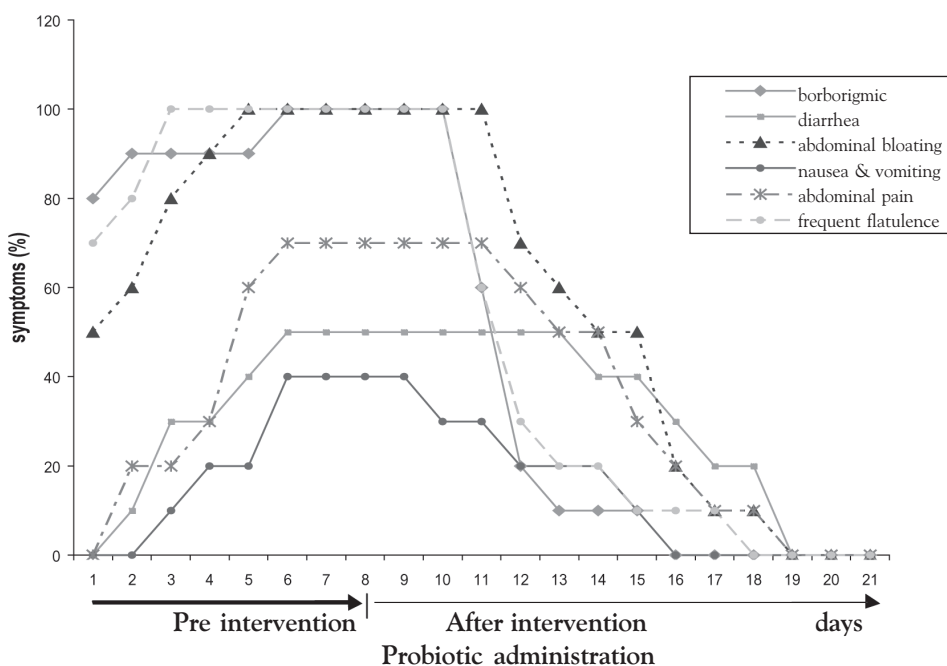


FIGURE 1. PERCENTAGE OF LACTOSE INTOLERANCE SYMPTOMS THAT OBSERVED DURING THE INVESTIGATION

toms of lactose intolerance were increasing from day 1 to day 7. After administration of probiotic these symptoms subsided or absent gradually until the end of the study. Lactose intolerance symptoms were diminished completely in 40 subjects at the end of the trial. Only 2 subjects still had clinical signs of lactose intolerance; 1 subject had frequent flatulence and 1 subject had abdominal bloating. Borborismic, nausea and vomiting were diminished at the 16th day; abdominal pain and diarrhea were recovered at the 19th day.

Table 1 shows the decreasing mean of symptom score before and probiotic administration. The results were statistically significant.

TABLE 1. LACTOSE INTOLERANCE SYMPTOMS SCORE BEFORE AND AFTER ADMINISTRATION OF PROBIOTIC

	Lactose intolerance symptom scores					p*
	Pre		After			
	7th day	14th day	21st day			
Mean (SD)	13.8 (5.5)	7.5 (3.5)	0.119 (0.55)			<0.001
Median (Range)	13.5 (5-21)	8.0 (2-15)	0.0 (0-3)			

p* *Friedman test*, followed with *Wilcoxon test*, 7th-14th day (P<0.001), 7th-21st day (P<0.001), 14th-21st day (P<0.001)

Table 2 shows that the clinical symptom scores before and after administration of probiotic were statistically significant except for comparison of diarrhea on 14th and 7th days.

At the end of the study 36 cases showed negative BHT result, while the remaining 6 cases showed positive BHT.

TABLE 2. RESULTS OF BREATH HYDROGEN TEST (BHT) BEFORE AND AFTER ADMINISTRATION OF PROBIOTIC

BHT	Before		After		p*
	n	%	n	%	
Positive (+)	42	100	6	14.3	<0.001
Negative (-)	0	0	36	85.7	

p* *Mc Nemar test* results (p<0.001)

Discussion

During the first 7 days of observation, each subject showed different symptoms of lactose intolerance. All subject at 7th day of observation showed the highest degree of symptoms of lactose intolerance (**Table 3**). There was no literature stated about chronological detail of symptoms of lactose intolerance. The onset of the symptoms that can be clearly seen after consuming lactose vary in each individual. Several factors played the role in this condition, namely: ^{5, 14-16}

1. The activity of lactase enzyme in the intestine. The lower the activity the higher the probability of lactose intolerance to occur.
2. The amount, the frequency, and the way the lactose is consumed. Symptoms usually not occur when it is consumed in lower amount, or in divided amount or consumed together with fat, for example drinking chocolate milk soon after meal.
3. Time of gastric emptying and transit time of lactose in the small intestine. The faster the gastric emptying and the faster it stays in the small intestine, the lower the amount of lactose that being hydrolyzed. The longer lactose stays in the colon the larger possibility of lactose intolerance to occur.

TABLE 3. DISTRIBUTION OF THE CLINICAL SYMPTOMS BEFORE AND AFTER ADMINISTRATION OF PROBIOTIC

Symptoms	Pre		After		Cochran test p*	Mc Nemar test		
	7th day	14th day	21st day	pm ₁		pm ₂	pm ₃	
	n (%)							
Borborismic	41 (97.6)	4 (9.5)	0 (0)	<0.001	<0.001	<0.001	0.025	
Frequently flatulence	42 (100)	9 (21.4)	1 (2.4)	<0.001	<0.001	<0.001	0.008	
Abdominal bloating	42 (100)	21 (50)	1 (2.4)	<0.001	<0.001	<0.001	<0.001	
Nausea and vomiting	15 (35.7)	7 (16.7)	0 (0)	<0.001	0.008	<0.001	0.016	
Abdominal pain	31 (73.8)	19 (45.2)	0 (0)	<0.001	<0.001	<0.001	<0.001	
Diarrhea	19 (45.2)	18 (42.9)	0 (0)	<0.001	1.000	<0.001	<0.001	

p* *Cochran test*, followed *Mc Nemar test* (pm)

pm₁ = 7th-14th day, pm₂ = 7th-21st day, pm₃ = 14th-21st day

4. Flora of the colon. The symptoms will occur when there is an adequate amount of bacteria to perform fermentation.
5. Sensitivity of the colon with acidification. The higher the colon's sensitivity or the lower the colon's ability to adapt acidification the larger the possibility of lactose intolerance to occur.

In a low activity of lactase enzyme in the small intestine, unhydrolyzed lactose will be continued to the colon. In colon some of the unhydrolyzed lactose will be fermented by flora of the colon to be short-chain fatty acid (butyric acid, propionic acid, acetic acid) and gases (hydrogen, carbondioxyde, methane, etc). These gases can cause borborigmic, flatulence, abdominal bloating, nausea or vomiting, and abdominal pain. Accumulation of lactose and its metabolite from fermentation process may increase osmotic pressure intra luminal of colon and will cause shifting of the intracellular fluid into the lumen. The latter will increase the peristaltic movement of the intestine and eventually will cause diarrhea.^{5, 14}

After given full cream milk fortified with probiotic for 1 week, most of the symptoms of intolerance was decreasing gradually; borborigmic 9.5%, frequent flatulence 21.4%, abdominal bloating 50%, nausea and vomiting 16.7%, abdominal pain 45.2%, and diarrhea 42.9%, but each subject still experience mild symptoms of lactose intolerance. The symptoms of lactose intolerance were disappearing completely after 2 weeks probiotic intervention mostly in 40 subjects. The symptoms of borborigmic, nausea, and vomiting disappeared on 16th day; abdominal pain and diarrhea disappeared on 19th day. How long each symptoms of lactose intolerance will disappear after consumption of lactose added with probiotic has never been discussed in the literature. Two children that were still having frequent flatulence and abdomen bloating in this study were caused by the sensitivity of colon bacteria to adapt gastrointestinal disturbance, and it is different individually.^{17,18}

Table 1 shows that there was a significant decrease in mean score of lactose intolerance symptoms of pre and after intervention in 1 as well as 2 weeks of administration of probiotic. Clinically, each subject still experienced lactose intolerance symptoms during 1 week administration of probiotic. Regarding the percentage of symptoms, **Table 2** showed that almost in all comparison of before and after administration of probiotic,

there was significant difference except symptom of diarrhea during 1 week of probiotic administration. The result showed that a two week probiotic administration is effective statistically as well as clinically in children who consumed full cream milk. This result is in accord with the previous study that consumption of yoghurt or fermented milk that contained probiotic in Paris can decrease the symptoms of lactose intolerance. In that study subjects were given yoghurt or fermented milk everyday for 2 weeks. The results showed that the symptoms of lactose intolerance decreased dramatically and were statistically significant.¹⁹

This study showed a significant difference of BHT results before and after 2 week administration of probiotic. This result is are in accord with those of the previous study by Savaiano *et al*²⁰ in Paris, France. Sixteen subjects, 20-33 years old, with lactose intolerance and positive BHT, after 2 weeks ingestion of probiotic (yoghurt), there were significant change in BHT results. Similar results were reported by Shermak *et al*.²¹ Consumption of probiotic in the form of yoghurt or other fermented milk improves lactose digestion by β -galactocydase (lactase enzyme). Furthermore, yoghurt or fermented milk has a higher viscosity and a lower pH and make the yoghurt leave the stomach slowly and lactose reach the colon slowly, and thus give longer time for lactose to be hydrolyzed in the small intestine.^{5,19-21} Therefore the concentration of breath hydrogen will decrease or become normal.

The scoring system applied in this study using a mean score from clinical manifestations attempted to make the results more or less objective. However, in this scoring system subjectivity can not be fully excluded, because of the variety in clinical signs in every participant.

In conclusion, our findings suggest that two weeks of probiotic therapy improves the symptoms of lactose intolerance in children who consumed full cream milk and is supported by the improvement of BHT.

References

1. Boediarso A. Perkembangan laktase dan hubungannya dengan makanan bayi. *Sari Pediatri* 1994;1:17-20.
2. Sunoto. Intoleransi laktosa. *Bahan Kuliah Bagian Ilmu Kesehatan Anak FKUI-RSCM, Jakarta*, 1991. p.1-6.

3. Zhong V, Priebe MG, Vonk RJ, Huang CY, Antonie JM, Harmsen HJ, *et al.* The role of colonic microbiota in lactose intolerance. *Dig Dis Sci* 2004;49:78-83.
4. Firmansyah A. Laktosa dan laktase, aspek biokimiawi dan laboratorium. Bahan Kuliah Bagian Ilmu Kesehatan Anak FKUI RSCM, Jakarta. p.1-10.
5. Buller HA. Lactase phlorizin hydrolase: A review of the literature [dissertation]. Netherland: University of Amsterdam; 1990. p.2-25.
6. Schmitz J. Malabsorption. In: Walker WA, Durie PR, Hamilton JR, editors. *Pediatric gastrointestinal disease*. St-Louis: Mosby, 1996. p.83-95.
7. Levine B. About lactose intolerance. *Nutr Tod* 1996;31:78-9.
8. Gilliland SE, Kim HS. Effect of viable starter culture bacteria in yoghurt on lactose utilization in humans. *J Dairy Sci* 1984;67:1-6.
9. More about lactose intolerance (editorial), [cited September 7, 2002] Available from: URL: <http://www.geocities.com>.
10. Fuller R. Probiotic in human medicine. *Gut* 1991; 32:439-42.
11. Reid G. Regulatory and clinical aspect of dairy probiotic. FAO/WHO expert consultation on evaluation of health and nutritional properties of powder milk with live lactic bacteria, 2001.
12. Ahmad R. Probiotik: Aspek kesehatan, keamanan, dan regulasi, SEAMEO-TROPMED Regional Center for Community Nutrition, Universitas Indonesia. Presented at Malam Klinik IDAI, 2002.
13. Martini MC, Savaiano DA. Reduced intolerance symptoms from lactose consumed during a meal. *Am J Clin Nutr* 1988;47:57-60.
14. Montes RG, Perman JA. Lactose intolerance. *Postgrad Med* 1991;89:175-84.
15. Young RJ, Huffman S. Probiotic use in children. *J Pediatr Health Care* 2003;17:277-283.
16. Kerzner B. Breath tests. In: Wyllie R, Hyams JS, editors. *Pediatric gastrointestinal disease patophysiology, diagnosis, management*. 9th ed. Philadelphia: WB Saunders, 1993. p.1027-37.
17. Vrese MD, Stegelmann A, Richter B, Frenselan S, Laue Ch, Schrezenmeir J. Probiotic-compensation for lactase insufficiency. *Am J Clin Nutr* 2001;73(suppl): 421s-9s.
18. Briet F, Pochart P, Marteau P, Flourie B, Arrigani B, Rambaud JC. Improved clinical tolerance to chronic lactose ingestion in subjects with lactose intolerance: a placebo effect? *Gut* 1997;41:632-5.
19. Martini MC, Lerebours EC, Jin Lin W, Harlander SK, Berroda NM, Antoine JM, *et al.* Strains and species of lactic acid bacteria in fermented milks (yoghurts): Effect on in vivo lactose digestion. *Am J Clin Nutr* 1991;54:1041-6.
20. Savaiano DA, Smith DE, Martini MC. Lactose digestion from flavored and frozen yoghurts, milk, and ice cream by lactase-deficient persons. *Am J Clin Nutr* 1987;46:636-40.
21. Shermak MA, Saavedra JM, Jackson TL, Huang SS, Bayless TM, Perman JA. Effect of yoghurt on symptoms and kinetics of hydrogen production in lactose-malabsorbing children. *Am J Clin Nutr* 1995; 62:1003-6.