A randomized trial of *Lactobacillus acidophilus* BG2FO4 to treat lactose intolerance[1–5]

John R Saltzman, Robert M Russell, Barbara Golner, Susan Barakat, Gerard E Dallal, and Barry R Goldin

ABSTRACT

Background: Lactose intolerance is the most common disorder of intestinal carbohydrate digestion. *Lactobacillus acidophilus* BG2FO4 is a strain of lactobacilli with properties of marked intestinal adherence and high β-galactosidase activity.

Objective: This study was designed to determine whether oral feeding of *Lactobacillus acidophilus* BG2FO4 leads to a lactose-tolerant state.

Design: We studied 42 subjects with self-reported lactose intolerance and performed breath-hydrogen tests to determine whether they were lactose maldigesters. Subjects with established lactose maldigestion ($n = 24$) were invited to be randomly assigned to an omeprazole-treated (hypochlorhydric) group or a non-omeprazole-treated group, but 6 subjects chose not to participate. All randomly assigned subjects ($n = 18$) ingested *Lactobacillus acidophilus* BG2FO4 twice per day for 7 d and stool samples were collected. Breath-hydrogen tests were performed and symptom scores were recorded at baseline and after lactobacilli ingestion.

Results: Lactose maldigestion was established in 24 of 42 subjects (57%) with self-reported lactose intolerance. In 18 lactose-maldigesting subjects, overall hydrogen production and symptom scores after ingestion of *Lactobacillus acidophilus* BG2FO4 were not significantly different from baseline values. Live *Lactobacillus acidophilus* BG2FO4 was recovered in stool samples from 7 subjects.

Conclusions: Lactose intolerance is overreported in subjects with gastrointestinal symptoms after lactose ingestion. Treatment of lactose-maldigesting subjects with and without hypochlorhydria with *Lactobacillus acidophilus* BG2FO4 for 7 d failed to change breath-hydrogen excretion significantly after lactose ingestion. *Am J Clin Nutr* 1999;69:140–6.

KEY WORDS Lactose intolerance, *Lactobacillus acidophilus*, breath-hydrogen test, omeprazole, hypochlorhydria, humans

INTRODUCTION

Lactose maldigestion is the most common disorder of intestinal carbohydrate digestion in humans. Although virtually all infants can digest the milk sugar lactose, there is a slow decline in lactase activity in childhood: ≈50% of African American children are lactose maldigesters by 12 y of age and adults of most ethnic groups are lactose maldigesters (1). Lactose maldigestion is due to the reduction or loss of lactase activity in the intestinal brush border. In select populations, the ability to digest lactose persists to adulthood, with a 90% prevalence of persistent lactose digestion in northern European whites (1). In the United States, ≈25% of adults are lactose maldigesters compared with 75% of adults worldwide (2, 3). Ingestion of lactose by a person with lactose maldigestion may lead to abdominal bloating, flatulence, and diarrhea.

Although most adults in the world are lactose intolerant, large quantities of yogurt are consumed by some of the lactose-maldigesting populations. The lactose ingested in yogurt is better digested than is the lactose in milk (4, 5). It is believed that the enhanced digestion of lactose in yogurt is a result of intraintestinal digestion of lactose by lactase released from yogurt-producing organisms, which only occurs if the culture is added after pasteurization. There is a reduction in the lactose content of yogurt during the fermentation process that varies with the length of storage time before ingestion. In addition, the duration of bacterial lactase activity corresponds with the duration of survival of lactobacilli after ingestion. The presence of gastric acid degrades the bacterial lactase activity in 20–60 min (6).

It has been hypothesized that ingestion of a strain of *Lactobacillus* with properties of high β-galactosidase activity and avid intestinal adherence would lead to prolonged intestinal survival

of lactobacilli and possibly the conversion from a lactose-intolerant to a lactose-tolerant state. *Lactobacillus acidophilus* BG2FO4 was selected to test this hypothesis because this organism has the ideal qualities of high lactase activity and strong intestinal adherence (7). Furthermore, we hypothesized that this strategy would be most effective in patients with hypochlorhydria because the organisms and enzyme would be more likely to survive passage through the stomach into the small intestine.

Healthy subjects with self-reported lactose intolerance were studied and actual lactose maldigestion was evaluated by measuring breath-hydrogen production after lactose ingestion. Subjects with documented lactose maldigestion were randomly assigned to an omeprazole-treated group (to induce hypochlorhydria) or a non-omeprazole-treated group. We used breath-hydrogen measurements after lactose ingestion to determine the degree of lactose maldigestion. We tested the hypothesis that ingestion of a strain of *Lactobacillus* with a high β-galactosidase activity and marked intestinal adherence would lead to prolonged intestinal survival of this organism in volunteers with a normal gastric pH, in individuals with gastric hypochlorhydria, or in both, and would result in a lactose-intolerant-individual becoming lactose tolerant.

SUBJECTS AND METHODS

Subjects

People who believed that they were lactose intolerant were recruited through advertisements at the Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University and in a Boston newspaper. The criteria used to recruit patients with self-reported lactose intolerance were as follows: *1*) subjects had reported one or more of the following symptoms after ingestion of milk or other dairy products: abdominal bloating, gas, abdominal pain or discomfort, and diarrhea, and *2*) subjects had eliminated milk and other dairy products from their diets. Potential participants had to be free of intrinsic factor antibodies and had to have normal hematologic indexes (white blood cell counts, hemoglobin, hematocrit, mean corpuscular volume, and platelet counts), normal serum albumin concentrations, and normal results from tests of liver (alkaline phosphatase, total bilirubin, and transaminases) and kidney (blood urea nitrogen and creatinine concentrations) function. Subjects were excluded if they had had gastric or intestinal surgery; drank excessive amounts of alcohol; had peptic ulcer disease, a small-intestinal disorder, or pancreatic disease; or were taking diazepam, H_1-blockers, antipyrine, phenytoin, warfarin, or theophylline. Subjects were given a stipend for their participation in the study. We obtained written, informed consent from all subjects under the guidelines established by the Human Investigation Review Committee of the New England Medical Center and Tufts University, Boston.

Lactose digestion

The ability of the study participants to digest lactose was determined by measuring their end-alveolar hydrogen concentrations 30 min after and then hourly for 4 h after ingestion of 20 g lactose and 100 mL water. The concentrations of hydrogen and carbon dioxide in breath samples were analyzed by gas chromatography (Microlyzer gas analyzer, model DP; Quintron Instruments, Milwaukee). Changes in breath-hydrogen concen-

trations were calculated by subtracting the baseline (fasting) hydrogen concentrations from subsequent test values. To correct the hydrogen values for atmospheric contamination of alveolar air, the observed carbon dioxide concentrations were normalized to 45 mm Hg (the partial pressure of carbon dioxide in alveolar air). Subjects were classified as having lactose maldigestion if their breath-hydrogen concentrations increased by >6 ppm (8).

During the study protocol, end-alveolar hydrogen concentrations were determined at 30 min and then hourly for 8 h after ingestion of 20 g lactose.

Reporting of symptoms

Subjects were asked to rate the presence and severity of gastrointestinal symptoms after each breath test (9). Abdominal pain, abdominal distention, abdominal bloating, and flatulence (gas) were ranked as follows: 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, and 3 = severe symptoms. Bowel movements were scored as 0 = none; 1 = 1 stool; and 2 = ≥2 stools. Stool consistency was scored as >0 = normal or firm, 1 = loose, and 2 = watery. The number of points for each category was totaled to determine the overall degree of symptoms.

Experimental protocol

All subjects who met the inclusion criteria underwent a 4-h breath-hydrogen screening after ingesting 20 g lactose. Only one subject was excluded during the screening process, because of a previous history of intestinal resection. Of the 42 subjects fulfilling the entry criteria, 24 (57% of screened subjects) were determined to have lactose maldigestion. The 18 subjects (43% of screened subjects) who did not have lactose maldigestion were not evaluated further. Eighteen of the 24 subjects (6 men and 12 women aged 39.7 ± 4.0 y) confirmed to have lactose maldigestion agreed to participate in the full study protocol; the other 6 chose not to participate because of concerns about potential discomfort from gastrointestinal intubations.

Subjects who met the screening criteria for lactose maldigestion were randomly assigned to the non-omeprazole-treated group (3 men and 7 women) or the omeprazole-treated group (3 men and 5 women). Omeprazole (Prilosec; Merck and Co, Inc, Westpoint, PA) was administered in a dosage of 40 mg once per day for 7 d to the omeprazole-treated group before the baseline breath-hydrogen tests and then was continued for the duration of the study. There was no placebo used and the study design was not blinded. All subjects were admitted to the Metabolic Research Unit of the Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University for study.

After an overnight fast, all subjects underwent an 8-h breath-hydrogen test after ingesting 20 g lactose. Questionnaires on symptoms were completed at the conclusion of the breath test. On day 2, after an overnight fast, all subjects began ingesting the contents of vials containing live *Lactobacillus acidophilus* BG2FO4 (1×10^{10} organisms/vial) twice per day. Ten subjects (6 in the non-omeprazole-treated group and 4 in the omeprazole-treated group) agreed to undergo gastrointestinal intubations. Twelve hours after the ingestion of a *Lactobacillus acidophilus* BG2FO4 vial, a mercury-weighted Entriflex tube (Bioresearch Medical Products, Inc, Somerville, NJ) fused to a Cecar pH microelectrode (Monocrystant Model 91-0011; Synectics Medical, Stockholm) was passed into the stomach. The pH electrode was attached to a pH meter (Synectics Digitrapper Mark II; Synectics Medical) and the output was continually measured.

The tube was then advanced to the area of the ligament of Treitz, and an intestinal fluid sample was obtained for bacterial cultures. Placement of the tube was confirmed by fluoroscopy.

The tube was withdrawn into the stomach and a pentagastrin stimulation test was performed (Peptavlon; Ayerst Laboratories, York, NY). We judged hypochlorhydria to be present when the peak acid output (PAO) after pentagastrin stimulation was <2.0 mmol/h and the maximal acid output (MAO) was <1.0 mmol/h. Basal acid output (BAO), PAO, and MAO were calculated from gastric fluid aspirate collections. Stool samples were obtained during the 7-d *Lactobacillus acidophilus* BG2FO4 treatment period for bacteriology studies.

After 7 d of ingestion of *Lactobacillus acidophilus* BG2FO4 and after an overnight fast, subjects ingested 20 g lactose and then an 8-h breath-hydrogen test was performed. The last *Lactobacillus acidophilus* BG2FO4 vial had been administered 12 h before the start of this breath test. At the conclusion of the breath-hydrogen test, questionnaires about symptoms were again completed.

Microbiology

Lactobacilli were maintained in 1-mL vials of skim milk at −80 °C. They were thawed immediately before use and not refrozen. The number of viable lactobacilli was determined by serial 10-fold dilution in phosphate-buffered saline (PBS; 0.8%, 0.1 mol/L, pH 7.2), and 0.1-mL aliquots were spread evenly on lactobacilli-selective (LBS) agar (BBL, Cockeysville, MD). Plates were incubated anaerobically at 37 °C for 48 h and then colony forming units (CFUs) were estimated. All vials were kept at −80 °C until 1 h before their administration to the study participants. The number of organisms per vial was confirmed to be $\geq 1 \times 10^{10}$.

The number of CFUs per liter in the intestinal aspirates and stool specimens was obtained by serial dilutions (1:10) in sterile 0.1 mmol PBS/L through the 10th dilution (-10^{10}). After being mixed, a 0.1-mL aliquot of each dilution was placed on 2 sets of blood agar plates. One set was incubated in an anaerobic chamber (5% carbon dioxide, 10% hydrogen carbon monoxide, and 85% nitrogen) for determination of anaerobes and the other was placed in a jar containing carbon dioxide for determination of facultative anaerobes at 37 °C for 48 h.

Intestinal aspirates as well as stool samples were analyzed for lactobacilli. Intestinal aspirates and stool specimens were plated on LBS agar and incubated anaerobically and in carbon dioxide at 37 °C for 48 h to determine the number of lactobacilli. The number of viable lactobacilli was determined by counting the LBS plates. Verification of the identity of the colonies was determined by Gram staining and then inoculating the presumed *Lactobacillus acidophilus* BG2FO4 colonies to MRS (de Man, Rogosa, Sharpe) broth (Difco Laboratories, Detroit) and incubating them anaerobically for 48 h. *Lactobacillus acidophilus* BG2FO4 grows heavily in the MRS broth and settles at the bottom, resulting in a clear supernate. Colonies that grew in the MRS broth were selected for biochemical testing with the api 50 CH system (Biometrieux, Hazelwood, MO). This system is used to determine sugar fermentation patterns, by using 50 different sugars, and to speciate latobacilli.

In addition, colonies with a biochemical profile similar to that of *Lactobacillus acidophilus* BG2FO4 underwent further testing to confirm whether the lactobacilli were of the *Lactobacillus acidophilus* BG2FO4 strain. (Pulsed-field gel electrophoresis fingerprint analyses were kindly performed on the lactobacilli isolates by DC Walker in the laboratory of Todd Klaenhammer at North Carolina State University.) Total DNA was digested with the restriction enzyme SMAI and separated in agarose under the following conditions: 22 h, 200 V, and 1–20-s switching times. Identification of a lactobacillus isolate as *Lactobacillus acidophilus* strain BG2FO4 required an SMAI pattern identical to that of known *Lactobacillus acidophilus* BG2FO4 organisms.

Statistics

Differences in changes in the area under the curves (trapezoidal rule) for breath-hydrogen concentrations between the omeprazole-treated and untreated subjects were evaluated by using repeated-measures analysis of variance (ANOVA). Gastric acid secretory characteristics were compared by using the Mann-Whitney U test because within-group SDs differed by an order of magnitude and levels reached zero in some omeprazole-treated subjects, precluding the use of a simple power-family transformation. SYSTAT version 5.0.3 (SPSS Inc, Chicago) was used for the analyses. The data are expressed as means ± SEMs.

RESULTS

The breath-hydrogen concentrations of the original 42 subjects with self-reported lactose intolerance after ingestion of 20 g lactose are shown in **Figure 1**. The 24 subjects whose breath-hydrogen concentrations increased by ≥6 ppm were classified as having lactose maldigestion. The 18 subjects whose breath-hydrogen concentrations increased by <6 ppm were classified as lactose digesters. Results of the gastric secretory tests (BAO, MAO, and PAO) of the subjects who volunteered for gastrointestinal intubation are shown in **Table 1**. All non-omeprazole-treated subjects ($n = 6$) had normal gastric secretory abilities and all omeprazole-treated subjects ($n = 4$) were confirmed to have hypochlorhydria as measured by BAO, MAO, and PAO.

Breath-hydrogen concentrations in the non-omeprazole-treated group before and 12 h after *Lactobacillus acidophilus* BG2FO4 ingestion for 7 d, after ingestion of 20 g lactose, are

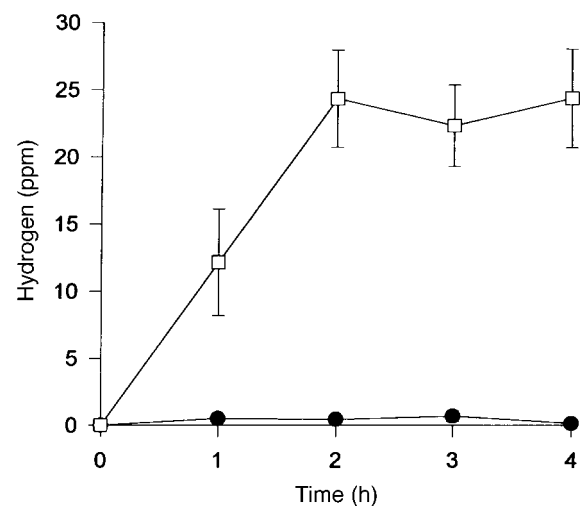**FIGURE 1.** Mean (±SEM) changes from baseline (fasting) in breath-hydrogen concentrations of 42 subjects after ingestion of 20 g lactose. Twenty-four subjects had lactose maldigestion as evidenced by a sizable increase (all >6 ppm) in breath-hydrogen concentrations (□), whereas 18 subjects had no increase in breath-hydrogen concentrations and could digest lactose (●).

TABLE 1
Gastric acid secretory characteristics of non-omeprazole-treated and omeprazole-treated subjects[1]

	Non-omeprazole-treated subjects ($n = 6$)	Omeprazole-treated subjects ($n = 4$)
Basal acid output (mmol·HCl^{-1}·h^{-1})	0.69 ± 0.17[2]	0.003 ± 0.003
Maximal acid output (mmol·HCl^{-1}·h^{-1})	10.96 ± 2.49[3]	0.72 ± 0.37
Peak acid output (mmol·HCl^{-1}·h^{-1})	15.70 ± 4.40[3]	1.13 ± 0.59

[1] $\overline{x}$ ± SEM.
[2,3] Significantly different from omeprazole treated (Mann-Whitney U test): [2] $P < 0.010$, [3] $P < 0.011$.

shown in **Figure 2**; those for the omeprazole-treated group are shown in **Figure 3**. In the non-omeprazole-treated group, the total area under the curve at baseline (126 ± 21 ppm/h) was not significantly different ($P = 0.47$) from that after *Lactobacillus acidophilus* BG2FO4 treatment (140 ± 16 ppm/h). In the omeprazole-treated group, the total area under the curve was not significantly different ($P = 0.19$) for the baseline test (74 ± 11 ppm/h) compared with after *Lactobacillus acidophilus* BG2FO4 treatment (154 ± 48 ppm/h), although the posttreatment breath-hydrogen curves tended to be higher. The posttreatment breath-hydrogen curves would have been lower if ingestion of *Lactobacillus acidophilus* BG2FO4 had resulted in effective lactose digestion.

Gastrointestinal symptoms after lactose ingestion before and after treatment with *Lactobacillus acidophilus* BG2FO4 are shown in **Table 2**. Overall, there were no significant changes from baseline in gastrointestinal symptoms (individual symptom scores or total scores) after treatment with *Lactobacillus acidophilus* BG2FO4 organisms.

Bacterial concentrations (CFU/L) of intestinal aspirates and stool samples in subjects treated with *Lactobacillus acidophilus*
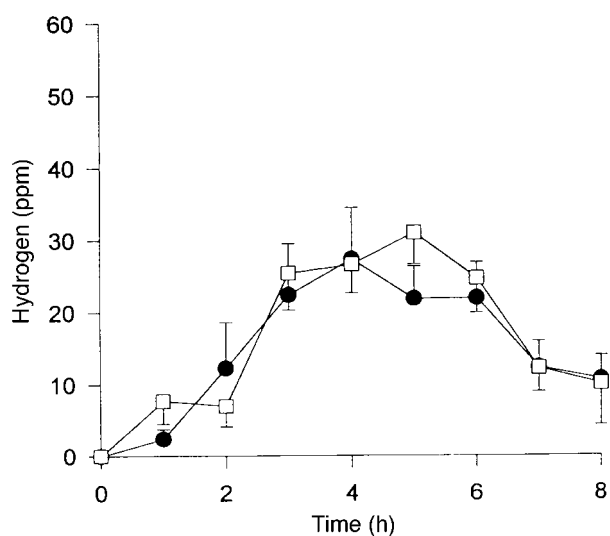
BG2FO4 with and without omeprazole treatment are shown in **Table 3**. Nine subjects (6 in the non-omeprazole-treated group and 3 in the omeprazole–treated group) underwent gastrointestinal intubations to obtain intestinal aspirates. As expected, subjects treated with omeprazole had significantly greater upper gastrointestinal bacterial overgrowth than non-omeprazole-treated subjects. Viable *Lactobacillus acidophilus* BG2FO4 was recovered in stool samples from 7 subjects (4 in the omeprazole-treated group and 3 in the non-omeprazole-treated group), none of whom were in the group that underwent gastrointestinal intubation. Viable *Lactobacillus acidophilus* BG2FO4 was not recovered in intestinal aspirates. Stool lactobacilli were confirmed to be *Lactobacillus acidophilus* BG2FO4 by pulsed field gel electrophoresis fingerprinting.

DISCUSSION

Although the organisms that make up the live cultures in yogurt are recognized to have lactase activity and contribute to the digestion of lactose, their length of survival is short and, typically, significant numbers survive for <60 min (4–6). The primary factors that limit the survival of lactobacilli within the upper gastrointestinal tract are gastric acid and the inherent ability of the organisms to adhere to intestinal epithelial cells (10). Lactase activity in yogurt was shown to drop by >80% at a pH of 5.0 in an in vitro model (11). In addition, long-term feeding of yogurt does not result in any significant change in the results of breath-hydrogen tests, indicating the absence of any significant prolonged intestinal survival by the yogurt organisms (6).

We sought to measure the potential prolonged survival of a unique strain of *Lactobacillus* and whether its long survival would result in a change in subjects from a lactose-intolerant to a lactose-tolerant state. Therefore, the *Lactobacillus acidophilus* BG2FO4 strain was selected for use in this study because it has

FIGURE 2. Mean (±SEM) changes from baseline (fasting) in breath-hydrogen concentrations of 10 lactose-maldigesting, non-omeprazole-treated subjects before (●) and 12 h after (□) treatment for 7 d with *Lactobacillus acidophilus* BG2FO4 after ingestion of 20 g lactose. Both groups of subjects had significant increases from baseline in breath-hydrogen concentrations.
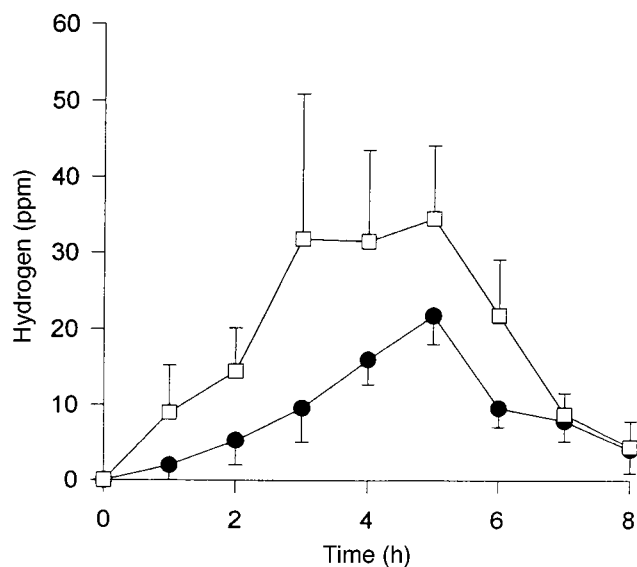
FIGURE 3. Mean (±SEM) changes from baseline (fasting) in breath-hydrogen concentrations of 8 lactose-maldigesting, omeprazole-treated subjects before (●) and 12 h after (□) treatment for 7 d with *Lactobacillus acidophilus* BG2FO4 after ingestion of 20 g lactose. Both groups of subjects had significant increases from baseline in breath-hydrogen concentrations; concentrations posttreatment tended to be higher than those before treatment, although not significantly so.

TABLE 2
Gastrointestinal symptoms in people with lactose intolerance before and after ingestion of 20 g lactose[1]

Group	Abdominal pain (0–3)	Abdominal distention and bloating (0–3)	Flatulence (gas) (0–3)	Bowel movements (0–2)	Stool consistency (0–2)	Total score (0–13)
Non-omeprazole-treated ($n = 10$)						
Baseline	1.0 ± 0.2	1.4 ± 0.3	1.9 ± 0.3	0.8 ± 0.3	0.8 ± 0.4	5.2 ± 0.7
Posttreatment	0.6 ± 0.2	1.1 ± 0.2	1.4 ± 0.2	0.9 ± 0.1	0.5 ± 0.2	4.4 ± 0.5
Omeprazole-treated ($n = 8$)						
Baseline	1.2 ± 0.4	1.6 ± 0.3	2.1 ± 0.2	1.0 ± 0.2	1.4 ± 0.2	7.0 ± 1.1
Posttreatment	1.2 ± 0.2	1.1 ± 0.3	1.7 ± 0.3	0.7 ± 0.3	1.0 ± 0	5.2 ± 1.1
Combined groups ($n = 18$)						
Baseline	1.1 ± 0.2	1.5 ± 0.2	2.0 ± 0.2	0.9 ± 0.2	1.2 ± 0.2	6.1 ± 0.7
Posttreatment	0.9 ± 0.2	1.1 ± 0.2	1.6 ± 0.2	0.8 ± 0.2	0.7 ± 0.1	4.8 ± 0.6

[1] $\overline{x} \pm$ SEM. Ranking of gastrointestinal symptoms is described in Methods. There were no significant differences between baseline and posttreatment values.

high β-galactosidase activity (7). In addition, the intestinal adherence of *Lactobacillus acidophilus* BG2FO4 in an in vitro model of human intestinal cells was the highest of 21 strains of human lactobacilli tested (7).

We further increased the chances for prolonged intestinal survival by eliminating gastric acid production in the omeprazole-treated group, as would be commonly found in elderly persons with atrophic gastritis. Atrophic gastritis occurs in 20–30% of healthy, elderly people and is the most common cause of reduced gastric acid secretion (12, 13). The lack of gastric acid often leads to bacterial overgrowth in the upper intestinal tract (14). Treatment with omeprazole, a potent inhibitor of gastric acid secretion that alters the activity of H^+/K^+-adenosine triphosphatase, induces a clinical state similar to atrophic gastritis with hypochlorhydria and frequent bacterial overgrowth (14–16). We used omeprazole in this study to heighten the chances of survival of *Lactobacillus acidophilus* BG2FO4 and β-galactosidase during passage through the stomach.

We found that *Lactobacillus acidophilus* BG2FO4 survived passage through the entire gastrointestinal tract, as evidenced by the presence of viable *Lactobacillus acidophilus* BG2FO4 in stool samples from 7 of 16 subjects. However, *Lactobacillus acidophilus* BG2FO4 was not detected in the upper intestine 12 h after ingestion, despite the avid properties of intestinal adherence of this organism and the lack of gastric acid in the omeprazole-treated group. This was reflected by the lack of improvement in overall breath-hydrogen excretion or changes in symptom scores after lactose ingestion. Subjects with viable *Lactobacillus acidophilus* BG2FO4 in stool samples had breath-hydrogen concentrations and symptom scores that were similar to those of the other subjects.

Negative data always raise the question of a type 2 statistical error, and the variability of our subjects' responses did not eliminate this possibility; however, we believe that it was unlikely because 11 of 18 of our subjects actually had an increase in breath-hydrogen excretion after treatment with *Lactobacillus acidophilus*

TABLE 3
Bacterial concentrations of gastric and intestinal aspirates and stool samples in subjects treated with *Lactobacillus acidophilus* BG2FO4 with and without omeprazole treatment[1]

Subjects	Intestinal aerobes	Intestinal anaerobes	Intestinal lactobacillus	Stool lactobacillus	Stool *Lactobacillus acidophilus* BG2FO4
			CFU/L		
Non-omeprazole-treated subjects					
1	1.0×10^6	1.0×10^6	0	ND	ND
2	1.0×10^5	2.0×10^5	0	ND	ND
3	4.0×10^7	5.0×10^7	0	0	0
4	1.0×10^6	0	0	3.0×10^{10}	0
5	1.0×10^5	0	0	3.8×10^9	0
6	0	0	0	0	0
7	ND	ND	ND	ND	0
8	ND	ND	ND	ND	5.0×10^8
9	ND	ND	ND	ND	5.0×10^{47}
10	ND	ND	ND	ND	8.0×10^{10}
Omeprazole-treated subjects					
1	1.0×10^7	3.0×10^7	0	3.0×10^{11}	0
2	3.0×10^{10}	1.0×10^{10}	4.0×10^6	2.0×10^{10}	0
3	0	3.0×10^6	3.0×10^5	1.8×10^7	0
4	ND	ND	ND	ND	3.7×10^{12}
5	ND	ND	ND	ND	1.9×10^{11}
6	ND	ND	ND	ND	4.0×10^{10}
7	ND	ND	ND	ND	0
8	ND	ND	ND	ND	2.0×10^{10}

[1] Zero values indicate $\leq 10^5$ CFU/L. CFU, colony-forming units; ND, not determined.

BG2FO4 rather than a decrease (Figure 3), which would have been expected if our treatment had resulted in effective lactose digestion. In addition, regardless of how we analyzed the data—original scale or logarithmic scale, repeated-measures ANOVA or analysis of covariance—the results showed no significant differences. Repeated-measures ANOVA of the raw areas under the breath-hydrogen curves gave the following P values: group-by-time interaction (0.234), group (0.489), and time (0.094).

Many people experience abdominal symptoms after food ingestion, including diarrhea, bloating, and flatulence. Although these symptoms commonly occur because of lactose maldigestion, they are not specific for lactose maldigestion. It has been suspected that many people who believe that they are intolerant of lactose-containing dairy products actually can digest lactose and have either normal postprandial sensations or other causes of abdominal discomfort (17, 18).

Although food ingestion causes many people to subsequently experience adverse abdominal symptoms, it is difficult to discern which component (if any) of the diet is responsible for the symptoms. Because lactose maldigestion is a common and well-recognized clinical entity, lactose maldigestion is frequently blamed for postprandial gastrointestinal symptoms (19). However, there is a large placebo effect that may account for improved symptoms in those who undergo dietary manipulations. In our study, we also evaluated whether patients with self-reported lactose intolerance actually had lactose maldigestion, as determined with the breath-hydrogen test. We found that 18 of 42 subjects (43%) with self-reported lactose intolerance actually did not have lactose maldigestion. We used the 4-h breath-hydrogen test as a screen for lactose maldigestion because it has been shown that virtually all lactose maldigesters will be detected within this time period (20, 21).

Suarez et al (22) performed a randomized, placebo-controlled, double-blind, crossover study of gastrointestinal symptoms in subjects with self-reported severe lactose intolerance. They found that people who considered themselves severely lactose-intolerant mistakenly attributed a variety of abdominal symptoms to lactose intolerance, including 9 of 30 subjects (30%) who did not have lactose maldigestion on the basis of the breath-hydrogen test. It is possible that our results may have underestimated the prevalence of lactose maldigestion because we measured only hydrogen and not methane production, and some of our subjects may have only produced methane. However, in the study by Suarez et al, all subjects found to be lactose digesters on the basis of the breath-hydrogen test produced hydrogen after ingestion of lactulose. It is estimated that the prevalence of non-hydrogen-producing subjects due to methanogenic colonic flora is nearly nil to >10%, with most studies suggesting that the most people are hydrogen producers (23). Thus, we suspect that few if any of the subjects in our study with normal results on the breath-hydrogen test were actually lactose maldigesters because they had only methane-producing colonic flora.

We conclude that lactose intolerance is overreported by subjects with gastrointestinal symptoms after lactose ingestion. We investigated the strategy of using organisms with β-galactosidase activity to colonize the upper gastrointestinal tract and to potentially convert a lactose-intolerant subject to a lactose-tolerant one. The study was designed to optimize the chances for an effective strategy by using subjects with hypochlorhydria and organisms with avid intestinal adherence properties combined with high β-galactosidase activity. However, ingestion of *Lactobacillus acidophilus* BG2FO4 for 7 d in subjects with lactose maldigestion with and without hypochlorhydria failed to result in any significant overall improvement in hydrogen production after lactose ingestion. The strategy of changing the enteric flora in the upper gastrointestinal tract to change an upper intestinal condition such as lactase deficiency does not appear to be effective.

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