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Lactose-free Yogurts do not Show any Benefits for Lactose-Intolerant Subjects, Compared with Lactose-Containing Yogurts

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Abstract

Nowadays, there is a constant increase in commercial lactose-free yogurts for lactose-intolerant individuals. However, the real interest of these yogurts is unclear considering that several clinical trials have shown that the living bacteria present in the yogurt improved lactose tolerance in hypolactasic subjects, due to their ß-galactosidase activity that remains functional in the small intestine of these individuals. The aim of this study was to determine whether the intake of Lactose-Free Yogurt (LFY) is beneficial for hypolactasic lactose-intolerant subjects compared with that of traditional, Lactose-Containing Yogurt (LCY). Twenty-two subjects with auto-reported digestive symptoms after milk consumption carried out a Hydrogen Breath Test (HBT) with 25 g lactose to confirm their hypolactasic status. Fourteen subjects (63.6%) who exhibit a positive HBT accompanied by digestive symptoms were finally incorporated into the study. In two independent days, they have to ingest, in a double-blind and randomized form, 250 g of LFY or LCY. These products brought 0.5g and 19.8 g of lactose, respectively and both exhibited total counts of lactic acid bacteria higher than 10^7 CFU/g. Changes in breath H_2 excretion and digestive symptoms were registered during 180 min. When the volunteers carried out the HBT with LFY and LCY, no differences were detected in H_2 excretion or the intensity of digestive symptoms (individual or total). Accordingly, our results suggest that the intake of LFY, that are more expensive than LCY, does not bring any supplementary detectable benefits for the lactose intolerant subjects.

Keywords

Yogurt; Lactose intolerance; Hypolactasia; Lactic acid bacteria; Hydrogen breath test; ß-galactactosidase

Introduction

Dairy products are considered as healthy foods due to their elevated content of proteins of high biological value, bioavailable calcium, B2, and B12 vitamins and short and medium chain fatty acids. Cow's milk also contains about 4.8-5.2 g/L of lactose, a disaccharide that is hydrolyzed in the proximal intestine by the brush-border enzyme lactase. This process releases glucose and galactose that are subsequently absorbed. Small intestine lactase is highly expressed at birth, allowing the newborn to digest the high amounts of lactose present in breast milk (~7 g/L). However, in about 65%-80% of the worldwide human population, lactase expression is genetically programmed to decrease from weaning, so that only a residual activity of this enzyme persists in the adult intestine [1]. The persistence of high levels of lactase activity in adults is due to the presence of Single Nucleotide Polymorphisms (SNPs) within the introns 9 and 13 of the mini-chromosome maintenance 6 (MCM6) genes, adjacent to the lactase gene [2]. Five different SNPs have been described in different populations in the world, that prevent the gradual inhibition of lactase expression induced by epigenetic events occurring after weaning and resulting in DNA methylation. This physiological decrease of lactase is called primary hypolactasia or primary lactase deficiency while the remnant individuals exhibiting one of the SNPs are considered lactase-persistent. Hypolactasic subjects may develop digestive symptoms including abdominal distension and pain, borborygmi, increased rectal gas and, in some cases, diarrhea, when they are consuming lactose-containing foodstuffs [3]. In these subjects, the malabsorbed lactose is fermented by the microbiota in the colon, producing gases (CO_2, H_2 and, eventually, CH_4) that diffuse across the intestinal wall into the bloodstream and are eliminated in the expired air. This phenomenon constitutes the physiological basis of the noninvasive Hydrogen Breath Test (HBT), widely used for the detection of lactose malabsorption, as an indirect reflection of hypolactasia [4]. However, most of the hypolactasic subjects can consume moderate amounts of milk (about 250-500 ml/d) without developing digestive symptoms. As the intestinal lactase is not inducible by its substrate in humans, this is more likely due to the metabolic adaptation of their colonic microbiota [5]. Cheeses and yogurts are better tolerated than milk by lactose-intolerant subjects. Indeed, most of the lactose-containing whey is eliminated during cheese processing, and the *Streptococcus thermophilus* and *Lactobacillus delbrueckii* sub sp. *bulgaricus* strains used for yogurt elaboration express a ß-galactosidase activity. Interestingly, this enzyme remains functional in the intestinal lumen of the hypolactasic subjects after yogurt intake, contributing to lactose hydrolysis and improvement of lactose tolerance [6]. Such findings have been confirmed by several clinical studies and based on this evidence; a health claim for yogurt was accepted by the European Food Safety Authority (EFSA) [7].

In this context, it is curious to note that, in recent years, the market for lactose-free dairy products, including yogurts, has been rapidly expanding around the world [8]. These products target individuals who frequently self-identify as lactose intolerant without any diagnostic test supporting their real status. Though the evidence suggests that Lactose-Free Yogurts (LFY) do not bring any specific benefits to the lactose intolerant individuals, compared with the Lactose-Containing Yogurts (LCY), no study was carried out to confirm it. Accordingly, the aim of this study was to compare breath hydrogen excretion and digestive symptoms in hypolactasic lactose-intolerant subjects after consuming LFY or LCY.

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Subjects and Methods

Ethics and subject recruitment

The study protocol was approved by the Ethics Committee for Research in Humans of the Faculty of Medicine, University of Chile, in compliance with the Helsinki Declaration. The subjects were carefully informed about the aims and procedures of the study and those who agree to participate and met the inclusion and exclusion criteria signed a written informed consent form.

Volunteers auto-reporting digestive symptoms after milk product consumption were invited to participate in the study through notices set in the campus of the Faculty of Medicine and on the online academic platform of the Faculty. Healthy subjects of both genera, <35 years of age, normal weight or moderately overweight, were recruited in the study. Exclusion criteria included pregnancy, the existence of chronic immune or metabolic diseases, antecedents of digestive surgery or digestive diseases including celiac disease and inflammatory bowel diseases, treatment with antibiotics or others drugs affecting the gastrointestinal tract during the month preceding the study.

Breath tests

A diagnostic HBT was carried out in the recruited subjects to confirm their hypolactasic status and lactose intolerance. With this aim, overnight (12 h)-fasted subjects had to go to the Dpt. of Nutrition (Faculty of Medicine, University. of Chile) at 08:30 am. They had to ingest 25 g of lactose dissolved in 250 ml mineral water. Breath samples were obtained by end expiratory sampling into 60 ml plastic syringes using a modified Haldane-Priestley tube, before ingestion of the test solution and at 30-minute intervals thereafter. The concentration of H_2 in breath samples (primary outcome) was measured using an electrochemical cell (Lactotest 102, MEC, Brussel, Belgium). Lactose maldigestion, as to reflect of the hypolactasic state of the subjects, was defined as an increase of more than 20 ppm in at least three consecutive breath samples. During the test, subjects had to register any occurrence of the following digestive symptoms (secondary outcome): abdominal pain, abdominal distension, borborygmus, diarrhea, and to grade each symptom as absent (0), mild (1), moderate (2), or severe (3). The total clinical index for digestive symptoms was calculated for each subject by summing the scores for each symptom (range 0-15), as previously described [9]. Subjects had to remain at rest during the duration of the test.

Subjects diagnosed as hypolactasic and lactose-intolerant, as indicated by the presence of digestive symptoms during the diagnostic HBT, were selected to perform the tests with LFY and LCY. For this, the overnight fasted volunteers had to assist the Department of Nutrition at 08:30 am on two independent days separated for at least 1 week. They had to ingest (in less than 10 min) 250 g of the tested products, LCY or LFY, that were administered in random order. The order of product attribution was determined by using a computer-generated list of random numbers and was assigned to each volunteer by a researcher who was not implicated in their recruitment and HBT realization. The yogurt was prepared by an independent person and both the volunteers and the researchers in charge of the collection and analysis of the breath samples were blinded with respect to the identity of the products (LCY or LFY). Breath samples were obtained at 30 min. of interval and digestive symptoms registered during the whole test, as previously described for the diagnostic test. The number of subjects participating in both tests was based on that used in the study of Kolars et al. [10].

Products

The nutritional composition (per 100 g) of the LFY was as follows: Energy: 93kcal; Proteins: 3.1 g; Fats: 2.8 g and Total carbohydrates:

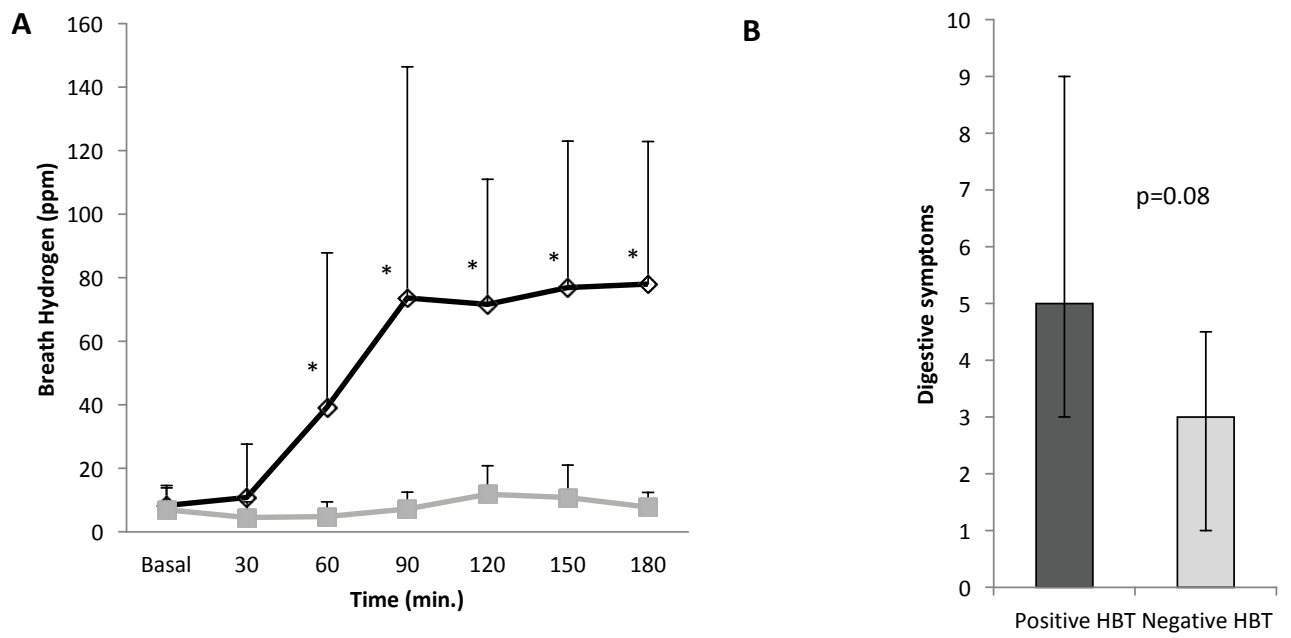

Figure 1: (A): Changes in breath hydrogen excretion (ppm) after the intake of 25 g lactose. Subjects were classified as hypolactasic (black line; n=14) when H_2 concentrations increased by more than 20 ppm over their basal values in at least 3 consecutives breath samples, or as lactose-persistent when it did not rise over 20 ppm (grey line; n=8) (Means ± SD). Both curves were compared through two-way ANOVA for repeated measurements (p=0.0017); significant differences were observed at each time from 60 min (*p<0.005). (B): Total digestive symptoms (Median [Interquartil range]).

13.9 g. The composition of LCY was similar: Energy: 97 kcal; Proteins: 3.5 g; Fats: 2.6 g and Total carbohydrates: 14.8 g. The lactose content, determined in our laboratory with a commercial assay kit (K-LOLAC 04/18, Megazyme, USA), was 0.14 ± 0.02 and 7.91 ± 0.71 g/100 g, respectively, in both products. As the volunteers had to eat 250 g of LFY and LCY yogurt when carrying out the HBT, the total amount of ingested lactose was approximatively 0.5 g and 19.8 g, respectively. Accordingly, approximately 40 times more lactose was ingested with LCY than with LFY. The number of lactic acid bacteria in the products was counted by culture in MRS and M17 agar for *Lactobacillus bulgaricus* and *Streptococcus thermophilus*, respectively. The total of lactic acid bacteria in both products was found to be higher than 10^7 CFU/g, as requested by the Chilean Food Regulation and Codex Alimentarius.

Statistics

Breath H_2 contents were shown as Means ± Standard Deviation and changes in this parameter during the test were compared between groups (hypolactasic/lactase-persistent) and products (LCY/LFY) by two-way ANOVA for repeated measurements. Digestive symptoms were expressed as Median and Interquartile Range and differences between groups (hypolactasic/lactase-persistent) and products (LCY/LFY) were determined by Man Whitney U test and Wilcoxon matched pairs test, respectively.

Results

Thirty subjects initially signed informed consent. However, two were excluded *a posteriori,* one for pregnancy and the other because he was erroneously classified as overweight when he was obese. Other six subjects decided to withdraw after evaluating that they would not have sufficient availability to perform all the tests. Accordingly, 22 subjects carried out the screening test with lactose. Hydrogen excretion increased by more than 20 ppm over basal values in at least 3 consecutive breath samples in 14 of them (63.6%) while it remained unaffected in the other 8 subjects, as shown in Figure 1A. The total digestive symptomatology tended to be higher (p=0.08) in the subjects with a positive HBT than in those with a negative HBT (Figure 1B). A significant positive correlation was observed between the total digestive symptoms and the total excreted H_2 at 120 min (r=0.57; p=0.006). The characteristics of the subjects with positive HBT were as follows: % Female: 78.6; Age: 23.9 ± 2.8 y.; Weight: 62.0 ± 8.6 Kg; Height: 162 ± 9 cm and BMI: 23.4 ± 2.0 Kg/m^2. These subjects were cited to carry out the tests with LFY and LCY. Results of the HBTs and the registered digestive symptoms are shown in Figure 2 and Table 1, respectively. No differences in breath H_2 excretion and in the individual and total digestive symptoms were detected between both products.

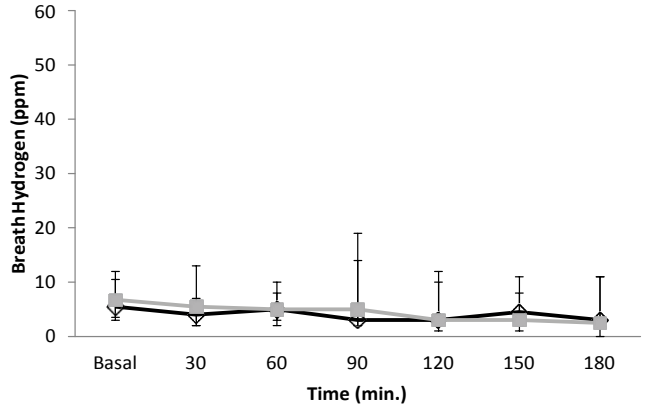

Figure 2: Changes in breath hydrogen excretion (ppm) after intake of 250 g of LCY (grey line) or LFY (black line) in fourteen hypolactasic volunteers (Median [IQR]). No significant differences were detected between both products (Two-way ANOVA for repeated measurements: p=0.73).

Table 1: Individual and total digestive symptoms reported by the volunteers after the intake of the LCY or LFY (Median [Interquartile range]). Individual symptoms were scored as absent (0), mild (1), moderate (2) and severe (3). The total digestive symptom index was calculated by summing the scores from each symptom and range from 0 to 15.

Symptoms	LCY	LFY	p
			(Wilcoxon matched pairs test)
Abdominal pain	0 (0-1)	0 (0-0)	0.18
Abdominal distension	0 (0-1)	0 (0-0)	0.18
Borborygmus	0 (0-1)	0 (0-0)	0.31
Rectal gas	0 (0-1)	0 (0-1)	1
Diarrhea	0 (0-0)	0 (0-0)	1
Total digestive symptom index	2.5 (1-4)	1 (1-3)	0.13

Discussion

The aim of this study was to determine whether it is justified, for lactose intolerant subjects, to consume lactose-free yogurts instead of traditional yogurts containing lactose. It is probable that lactose intolerance is currently overestimated in the population, as many individuals self-diagnose lactose intolerance without any diagnostic test supporting their real status. Accordingly, these subjects could wrongly attribute their gastrointestinal symptoms to lactose intolerance when, for example, they suffer from undiagnosed Irritable Bowel Syndrome (IBS) or other disorders. In our study, hypolactasic, lactose-intolerant subjects were carefully selected, based on an HBT with 25 g lactose, and taking as selection criteria an increase of breath H_2>20 ppm over baseline and the simultaneous report of digestive symptoms. Subsequently, the selected subjects had to ingest 250 g of LCY or LFY, i.e. an amount corresponding approximately to two commercial yogurts. The amount of lactose present in the LCY was high (7.9%, i.e. higher than in cow's milk) likely due to the fact that, as specified in the ingredient list appearing on the yogurt container, milk powder is added during the process of yogurt elaboration. Despite this high lactose content, our results show that the excretion of H_2 by the volunteers during the HBT with LCY did not differ from that observed after consuming the LFY. In addition, the presence and severity of the individual and total digestive symptoms during the test with the LCY did not differ either from those reported with the LFY. These results confirm the study from Kolars et al., described yogurt as an "autodigesting source of lactose", referring to the lactose-hydrolyzing ß-galactosidase expressed by the yogurt lactic acid bacteria [10]. Subsequently, more than 14 clinical studies described similar findings, showing that the intake of yogurt with living lactobacilli and streptococci decreases H_2 excretion as well as digestive symptoms, improving lactose tolerance in hypolactasic intolerant subjects [7]. Noteworthily, Marteau et al., using a naso - ileal perfusion technique, reported that less lactose was recovered from the terminal ileum of hypolactasic subjects after the ingestion of 18 g of lactose in yogurt with living bacteria than after that of the same amount of lactose in heated yogurt (with dead bacteria) [6]. About 20% of the yogurt bacterial lactase activity was detected in the terminal ileum and more than 90% of the ingested lactose was hydrolyzed in the

small intestine of these subjects, suggesting that the lactase activity contained in the viable starter culture contributed to the improvement of lactose tolerance [6]. The fact that, in our study, no increase in breath H_2 was observed after LCY means therefore that no significant amounts of lactose are reaching the colon to be fermented by the microbiota. Accordingly, the ß-galactosidase activity of the lactic acid bacteria present in the YCL was sufficient to hydrolyze most of the lactose in the small intestine of the hypolactasic subjects. Another factor, the gastrointestinal transit time, also contributes to the fact that yogurt lactose is better tolerated than milk lactose. Indeed, it is slower for yogurt (that is more viscous) than for milk [6], being the time of contact of lactose with the residual lactase present in the intestine of hypolactasic subjects, higher for yogurt than for milk, resulting in improved digestion. In relation with this point, the intake of lactose-containing yogurt elaborated with whole milk will be better tolerated that than that with skimmed milk, as dietary fat slows down gastric emptying. The same is observed when yogurt is ingested in the context of a complex meal, which also results in a slower gastric emptying. One limitation of our study is the strong inter-individual variability in the reporting As a result, we cannot ignore that a subset of subjects might be more sensitive to the presence of lactose in their small intestine, which is difficult to detect because of the relatively small number of subjects included in our study. It should, therefore, be advisable for these subjects to prefer yogurt made with whole milk, and ingested together with other foods.

Conclusion

In conclusion, our results indicate that, compared with LCY, the consumption of LFY does not bring any significant benefits for the lactose intolerants subjects. This is a relevant finding considering that compared with their lactose-containing counterparts; the lactose-free dairy products are generally more expensive and frequently exhibit an altered taste [11,12].

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