

ORIGINAL ARTICLES—ALIMENTARY TRACT

Subjective Perception of Lactose Intolerance Does Not Always Indicate Lactose Malabsorption

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BACKGROUND & AIMS: Symptomatic lactose intolerance is common; however, abdominal symptoms that patients experience after ingestion of lactose-containing foods can have causes beyond lactose malabsorption. We aimed to determine whether symptoms that patients usually attribute to lactose intolerance are comparable to symptoms provoked by a controlled lactose challenge and whether these symptoms are related to lactose absorption capacity. **METHODS:** We performed an observational, prospective, transverse study of 353 patients referred for a lactose hydrogen breath test (HBT). Patients completed a validated questionnaire about symptoms associated with consumption of dairy products at home (home symptoms). After a 50-g lactose breath test, they completed the same questionnaire again (lactose challenge symptoms). Patients were assigned to groups of absorbers or malabsorbers according to HBT results and tolerants or intolerants according to the results of the questionnaire. **RESULTS:** The total symptom score was significantly higher for home symptoms than for the lactose challenge (16 vs 8, $P < .01$). Symptoms perceived at home were reported to be more intense than those that followed the lactose challenge for lactose absorbers compared with malabsorbers (16 vs 4, $P < .01$) and lactose tolerants compared with intolerants (12 vs 2, $P < .05$). Overperception of lactose intolerance at home was similar in men and women. **CONCLUSIONS: Daily life symptoms that patients associate with lactose intolerance are often unrelated to lactose malabsorption. Even among true lactose malabsorbers, symptom recall tends to be amplified by the patient. Thus, conventional anamnesis is a highly unreliable tool to establish symptomatic lactose malabsorption.**

Keywords: Lactose Intolerance; Lactose Malabsorption; Hydrogen Breath Test; Lactase Activity.

Adult lactase deficiency and lactose malabsorption are common, but their relation to chronic abdominal symptoms is often unclear. In proven lactose malabsorbers, lactose challenge produces stereotyped symptoms that include abdominal distention, flatulence, abdominal cramping, and diarrhea, independently of whether lactose malabsorption is due to congenital, primary, or secondary lactase deficiency.¹ Symptoms of lactose intolerance are, at least in part, related to the amount of unabsorbed lactose but not necessarily to the magnitude of intestinal lactase activity. In this respect, it has been previously observed that symptoms of lactose malabsorption are not directly correlated with intestinal lactase activity^{2,3} or with the

magnitude of hydrogen production after a lactose load.⁴⁻⁶ The discrepancy between lactose intolerance symptoms and lactase activity might be due to a number of factors that can influence the symptomatic perception of lactose intolerance, such as lactose load, amount of lactose unabsorbed, type of administration (milk is different than lactose with water), consumption of lactose during a meal, gastric emptying, small bowel transit, colonic water absorption capacity, effect of colonic bacterial fermentation, or visceral sensitivity.⁷⁻⁹

Lactase-deficient persons tend to avoid dairy products because of the symptoms produced by incomplete digestion of lactose, even though proven lactase-deficient individuals might tolerate up to 7-12 g of lactose daily without noticeable effects.^{4,10} More commonly, individuals associate ingestion of lactose-containing products with their abdominal symptoms, but without objective evidence of insufficient lactase activity. In this respect, self-reported milk intolerance in patients with irritable bowel syndrome (IBS) is much more frequent than predicted by the lactose breath test, rendering symptoms somewhat unreliable for the purpose of identifying lactose malabsorbers.¹¹ Individuals who attribute their abdominal symptoms to lactose ingestion tend to avoid dairy products, an attitude that might have negative health implications such as favoring the development of osteoporosis in postmenopausal women.^{12,13}

The aim of the present study was to evaluate the reproducibility of self-reported lactose intolerance symptoms as perceived in the usual home conditions and after a lactose challenge. Our hypothesis was that lactose maldigestion might be often overrated by patients who associate their abdominal symptoms with dietary lactose. To this end, symptoms believed to be caused by lactose intolerance were evaluated in a group of patients who filled out a validated questionnaire about symptoms perceived under usual conditions at home and after a large oral load of 50 g of lactose.

Methods

Experimental Design

Three hundred fifty-three white patients (113 men, 240 women; median age, 41 years) referred to our Digestive System

Abbreviations used in this paper: HBT, hydrogen breath test; IBS, irritable bowel syndrome.

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Research Unit for evaluation of suspected lactose maldigestion by a hydrogen breath test (HBT) with lactose were prospectively studied after providing informed consent. None declined to participate in the study, had history of gastrointestinal surgery, or had taken antibiotics or been prepared for radiologic or endoscopic examinations for at least 2 weeks before entering the study.

Patients completed the validated questionnaire on lactose intolerance symptoms twice. First, before the lactose HBT, they were asked about symptoms they related to usual consumption of milk-based products at home (home symptoms). Second, at the end of the lactose HBT, they were asked about symptoms they might have experienced after the ingestion of a 50-g lactose test load (lactose symptoms). The standard 50-g lactose dose, equivalent to 1 L of milk, was chosen because it discriminates between lactose absorbers and malabsorbers on the basis of hydrogen production.¹⁴

Procedure

Hydrogen breath test. The 50-g lactose HBT was performed as described previously.¹⁴ Briefly, after a standardized low-carbohydrate dinner, overnight fast, and thorough brushing of the teeth, end-expiratory breath samples were obtained before and at 30-minute intervals after the 50-g lactose load at room temperature¹⁵ for the ensuing 3 hours. If a significant increase in hydrogen in breath was absent, sampling was extended to 5 hours. Breath samples were collected in hermetic bags fitted with a 3-way valve (GaSampler; Quintron Instruments, Milwaukee, WI). During the test, patients were instructed to remain seated. Eating, smoking, and exercising were not allowed during the test.

Hydrogen concentration was determined in breath samples by chromatographic analysis (Quintron model 12i Microlyzer; Quintron Instruments) and expressed as maximal increase over baseline concentration in parts per million. A positive test was defined as an increase in hydrogen above basal levels greater than 25 ppm.¹⁴ That cutoff was chosen because it has been validated for a 50-g lactose HBT, with a sensibility of 95% and specificity of 67%.¹⁴

Symptom questionnaire. A validated self-administered questionnaire for lactose intolerance was used for symptom assessment.¹⁶ The questionnaire includes 5 items related to symptoms most frequently reported by lactose-intolerant patients (diarrhea, abdominal cramping, vomiting, audible bowel sounds, and flatulence). Symptom severity was self-rated by

subjects on a 10-cm visual analogue scale ranging from 0 (without symptoms) to 10 (maximum symptoms). The total score on the questionnaire was obtained as the sum of the individual results of the 5 visual analogue scales. Thus, the total score on the symptom test ranged from 0 to 50.

Statistical Analysis

According to the Kolmogorov-Smirnov test, some values of the HBT did not conform to normality. Thus, variables were described as median and 25%-75% quartiles. Differences between medians were calculated with the Wilcoxon signed rank test or the Kruskal-Wallis analysis of variance test. Effect size of the questionnaire was calculated as the Cohen *d* (difference between the means, $M_{\text{home}} - M_{\text{lactose}}$, divided by the standard deviation of either group).¹⁷

Results

Lactose Breath Test Assessment

Lactose HBT result was abnormal, delta increase over 25 ppm, in 164 of the 353 patients (46.4%). These patients were classified as lactose malabsorbers. Age and female predominance were similar in lactose absorber and malabsorber groups.

Perception of Lactose Tolerance

Results of each individual item and total score on the home and lactose symptoms questionnaire are shown in Figure 1. All items except vomiting scored significantly higher in the home questionnaire than in the lactose challenge questionnaire. Consequently, the questionnaire total score was much higher when used for the assessment of symptoms perceived at home than for symptoms experienced after the test lactose load (16 [8-26] vs 8 [2-18], $P < .01$). Thus, although the 50-g lactose challenge elicited symptoms in many patients, self-perception of intolerance was much higher when recalling symptoms perceived previously under ordinary home conditions. The characteristics of home symptoms and lactose symptoms were nevertheless quite similar. Vomiting was the lowest scored item ($P < .01$) and flatulence the highest scored in home-perceived symptoms ($P < .01$).

The effect size of the total score allowed by the questionnaire was calculated to evaluate the magnitude of the difference in the scoring of the home and lactose symptom questionnaires. The effect size was 0.54, which corresponds to a medium effect size.

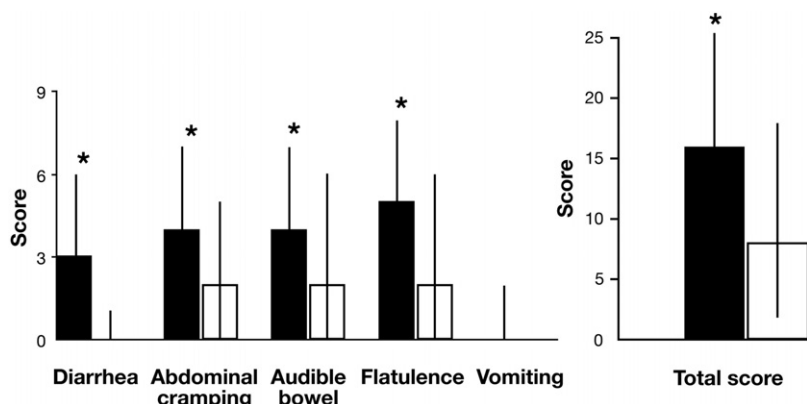


Figure 1. Results of the home symptoms questionnaire (black columns) and the 50-g lactose challenge questionnaire (white columns). Results are expressed as medians and 25th-75th percentiles. All items in the questionnaire except vomiting were scored significantly more highly at home than after lactose challenge. * $P < .01$.

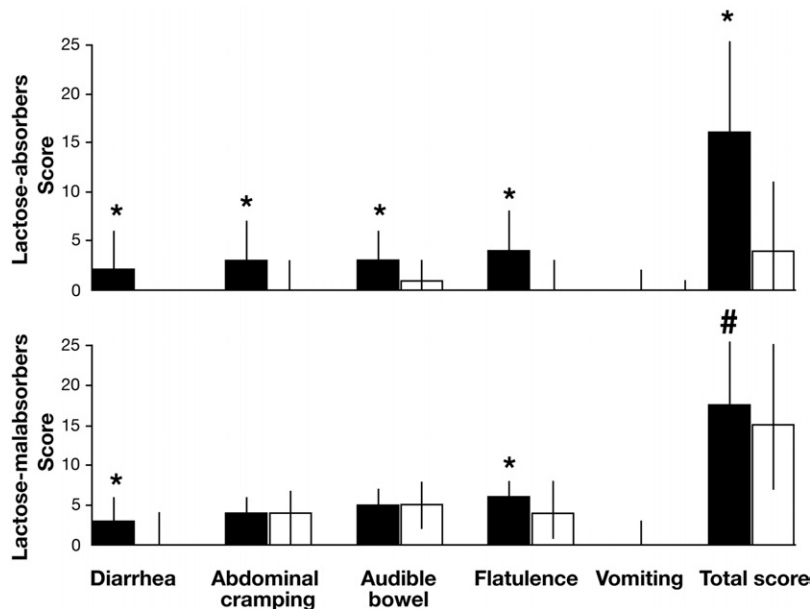


Figure 2. Results of the symptom questionnaire according to lactose absorption status as established by lactose HBT. *Upper figure* represents the results of each item and total score obtained in lactose absorbers, and *lower figure* represents these results in lactose malabsorbers. Results of home symptoms are represented in *black columns* and those recorded after 50-g lactose challenge in *white columns*. Results are expressed as medians and 25th–75th percentiles. Note that home symptoms are highly scored regardless of lactase status. * $P < .01$; # $P < .05$.

To assess the influence of true lactase deficiency on symptoms, we compared the results of the home and lactose challenge questionnaires on lactose absorbers and malabsorbers (Figure 2). In the 164 lactose malabsorbers, the individual lactose challenge scores were similar to those obtained on the home questionnaire. However, as a result of the increased reporting of diarrhea and flatulence at home, the total score on the questionnaire was significantly higher for home-recalled symptoms than after the lactose challenge. These differences were much more pronounced in patients with normal HBT, who showed home questionnaire scores consistently higher than on the lactose challenge questionnaire. Thus, lactose absorbers reported much more severe symptoms at home than after the lactose test load, suggesting that lactose malabsorption must play a relatively minor role in the symptoms that patients attributed to consumption of dairy products at home. Consistent with this observation is the fact that the total score on the lactose challenge questionnaire was significantly higher in patients with true lactose malabsorption than in patients without lactose malabsorption (15 [7–25] vs 4 [0–11] in lactase absorbers, $P < .05$). Conversely, the total score on the home questionnaire in patients with normal lactose absorption was similar to that in those with lactose malabsorption (15.5 [0–6] vs 16 [0–6], $P = \text{NS}$). The inconsistent correlation between home symptoms and lactose malabsorption is also indicated by a non-significant correlation between total score of home symptoms and increase in hydrogen production (Spearman rank order correlation = 0.06, $P = \text{NS}$). On the contrary, lactose symptoms experienced during the breath test were significantly correlated with the measured increase in hydrogen production (Spearman rank order correlation = 0.44, $P < .01$).

Relation Between Perceived Tolerance to Lactose Challenge and Previous Clinical Symptoms

To determine the influence of self-perceived tolerance versus non-tolerance to lactose on symptom scores, results of

the home and lactose questionnaires were compared separately in tolerants (defined as patients with a total score on the lactose challenge questionnaire ≤ 7 , the cutoff defined in the validation of the questionnaire) and intolerants (those with a total score on the lactose questionnaire > 7). Lactose intolerants scored previous symptoms at home and in response to the lactose test load following a similar individual symptom pattern, although total scoring on the home symptom questionnaire was significantly higher than after the lactose challenge (Figure 3). It is remarkable that patients self-defined as lactose tolerants on the basis of the lactose challenge test reported significantly much greater differences between home scores and lactose scores than did lactose-intolerant patients. These results suggest that despite patient manifestations, symptoms experienced at home were unlikely to be directly related to lactose-containing foods. To confirm this apparent lack of a relationship between home symptoms and true lactose malabsorption, the ratio of positive lactose HBT was compared among patients with a home questionnaire score greater than 7 and patients with a lactose questionnaire score greater than 7. Of the 185 patients with a lactose challenge score greater than 7, 119 (64.3%) had a positive lactose HBT. Interestingly, the number of positive lactose HBT results among the 271 patients with a home questionnaire score higher than 7 was significantly lower ($n = 135$ [49.8%], $P < .001$).

Assessment of Gender Influence

Questionnaire scores of 240 women and 113 men were compared to determine whether gender influences perception of lactose intolerance. As shown in Figure 4, both men and women scored home-perceived symptoms significantly higher than lactose challenge symptoms. The lack of influence of gender on lactose intolerance symptoms was further confirmed by the similarity of home and lactose questionnaire scores between men and women (Figure 4).

Discussion

There is extended belief among patients with abdominal symptoms that these are caused by lactose in dairy

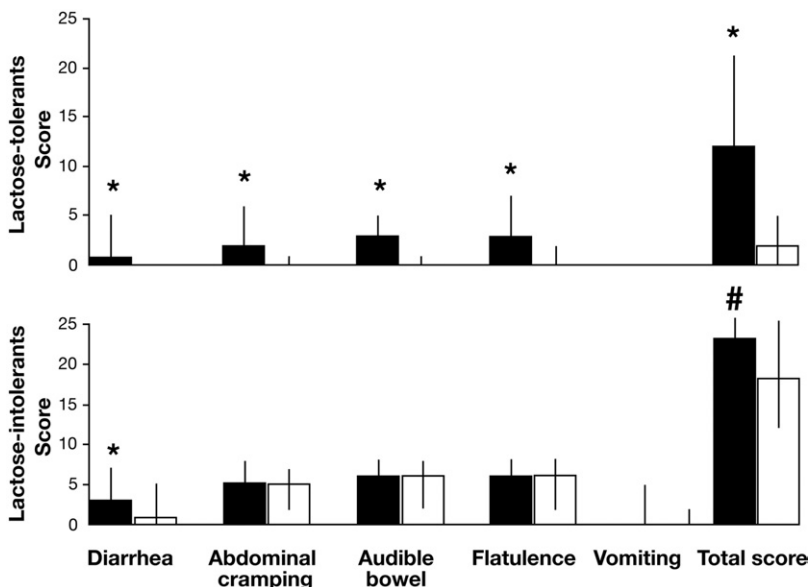


Figure 3. Results of the questionnaire according to lactose tolerance established by symptom response to 50-g lactose challenge. *Upper figure* represents the results of each questionnaire item and total score in lactose tolerants, and *lower figure* represents these results in lactose intolerants. Results of home symptoms are represented in *black columns* and those after 50-g lactose challenge in *white columns*. Results are expressed as medians and 25th–75th percentiles. Note that home symptoms were scored more highly by lactose tolerants. * $P < .01$; # $P < .05$.

products. Indeed, lactose-free milk and related food products have become quite successful commercially. Lactase deficiency in adults is indeed relatively common among the Western population, but enzyme deficiency and symptomatic lactose intolerance are not tightly correlated. When individuals think that they are intolerant to lactose, they tend to avoid dairy products.¹⁸ However, when lactose maldigestion is specifically screened by functional tests such as HBT or measuring intestinal lactase, evident discordances arise between objective determinations of lactase activity and symptoms of intolerance.^{2–6,19} Thus, it is generally considered difficult to predict lactose malabsorption from symptoms. To improve our understanding of the complex relationship between symptoms and lactose malabsorption, we undertook the present study that aimed to measure the symptoms self-reported by patients when consuming dairy products at home and compare them with the symptoms elicited by a

high-dose 50-g lactose challenge, by using a validated short 5-item symptoms questionnaire. Patients were grouped as lactose absorbers/malabsorbers depending on the result of 50-g lactose HBT (cutoff, 25 ppm) and as lactose tolerant/intolerant depending on the result of the total scale of the questionnaire (cutoff of 7 on the symptom scale after 50 g of lactose).

Our results confirmed the discrepancy between symptoms our patients attributed to lactose intolerance and symptoms elicited by a large lactose load in the laboratory. The classic study of Suarez et al (4) clearly showed that people who identify themselves as severely lactose-intolerant might mistakenly attribute a variety of abdominal symptoms to lactose intolerance. The present study expands these observations by comparing the intensity of symptoms experienced by patients who believe they are lactose-intolerant in their normal home setting and after ingesting a predetermined dose of lactose in the controlled phase of the study, ensuring that true lactose malabsorbers will develop symptoms during the test.⁴ Although one would think that symptom intensity has to be greater after a large lactose load than in daily life at home, our study showed just the opposite. Symptoms were perceived as more intense at home. A sensible explanation for this observation might be that symptoms patients believe related to lactose are aggravated by the home environment or, more likely, are not due to lactose malabsorption but to other causes. This latter explanation is supported by our observation that lactose absorbers with normal lactose HBT result had much higher scores on the symptoms questionnaire at home than after the lactose test. It is also conceivable that patients at home ingest lactose with other nutrients such as fat that could themselves cause symptoms. This possibility cannot be excluded by our study. One factor that, according to our results, did not significantly influence symptom perception was gender, because scoring on the symptoms questionnaire for men and women and referral to overperception of symptoms at home were similar.

IBS might be a key confounding factor. IBS is common, and its clinical expression, particularly diarrhea-predomi-

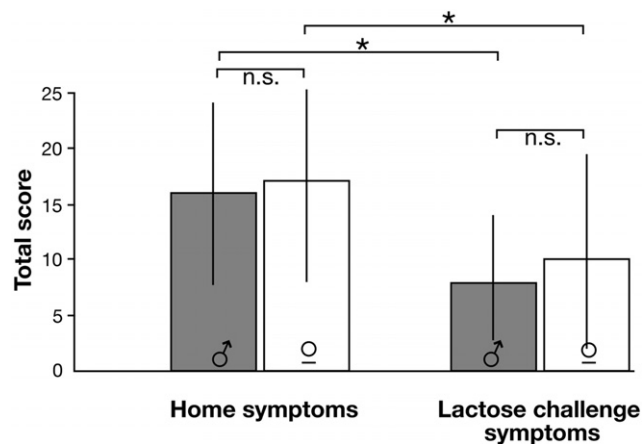


Figure 4. Influence of gender on scoring of symptoms questionnaire. Men’s results are represented in *gray columns* and women’s results in *white columns*. Results are expressed as medians and 25th–75th percentiles. Home symptoms are scored more highly than symptoms after lactose challenge regardless of gender. * $P < .05$.

nant IBS involving loose stools, cramps, bloating, and flatulence, resembles the symptoms that might be produced by lactose malabsorption. Furthermore, IBS patients might be particularly hypersensitive to lactose compared with healthy individuals²⁰ and might develop symptoms when challenged with oral lactose-free milk.²¹ Thus, patients with IBS might tend to associate abdominal symptoms with lactose ingestion, ascribing complaints to lactose maldigestion²² and eliciting from their physicians a referral for laboratory testing of possible lactase deficiency. Such patients might describe more intense symptomatology at home than in response to an acute lactose test load, as was the case for our study population. Although unlikely in the context of our study, we cannot fully exclude the potential confounding effects of overlooked conditions such as celiac disease or inflammatory bowel disease that cause symptoms resembling those of lactose malabsorption and that are associated with perceived lactose hypersensitivity and avoidance of lactose-containing foods.^{23,24}

A further point analyzed in the present study was whether the home symptoms of perceived lactose intolerance differ between patients who tolerated the ingestion of 50 g lactose versus those who were intolerant of the challenge. To this end, those patients who scored 7 or less on the total lactose challenge questionnaire were classified as tolerants.¹⁶ Surprisingly, tolerants did report significantly worse symptoms at home than after the 50-g lactose load. These results further suggest that symptoms attributed to lactose intolerance, which motivated referral to our diagnostic laboratory for possible lactase deficiency in the first place, are unrelated to lactose content in the diet. The lack of an apparent relationship between symptoms, lactose consumption, and lactase activity is in line with the literature, summarized in a recent meta-analysis.²⁵ Unfortunately in that analysis, there was insufficient variation in the study doses to establish a reliable dose-response relationship.

The relevance of our observations relates to 2 aspects. The first is that the lactose HBT as conventionally performed provides information on the capability of the bowel to digest lactose but does not necessarily clarify the origin of the clinical symptoms as obtained by the clinical history. The second is that restriction of normal amounts of dairy products with the consequent risk of dietary calcium deficiency is unwarranted in most patients, even those with a positive HBT in response to a high-load lactose challenge. A record of symptoms does not suffice to establish lactose malabsorption; specific procedures such as the lactose breath test should be performed to confirm it.

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Reprint requests

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Conflicts of interest

The authors disclose no conflicts.

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