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Symptoms of "lactose intolerance"

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ABSTRACT

Factors affecting or confounding the symptoms of lactose intolerance were examined by us in randomised, placebo-controlled and double-blind studies on healthy adult subjects. Evaluation of the diagnostic methods of lactose intolerance showed that cut-off values, according to the blood glucose values, varied widely. This result was based on a postal questionnaire, sent to all Finnish health centres. Symptoms were seldom recorded for a sufficiently long period. In carefully diagnosed lactose intolerant subjects, there was no difference in the severity of reported symptoms between ingestion of 0, 0.5, 1.5 and 7 g of lactose. Lactose maldigesters reported more severe symptoms after ingestion of lactose, but also sucrose, lactulose and fructo-oligosaccharides than controls. There was a strong relation among the reported symptoms in lactose intolerance, irritable bowel syndrome, the experience of abdominal pain in childhood, and female sex.

Key words: Lactose intolerance, lactose maldigestion, symptoms

Wide variations in the testing of lactose intolerance

Lactose digestion can be studied using either direct or indirect methods. The only direct methods are jejunal biopsy for the measurement of mucosal disaccharidases using intestinal intubation, proposed as the reference method, and an intestinal perfusion technique for the exact measurement of lactose digestion. The indirect methods include the breath hydrogen test, the measurement of breath $^{13}CO_2$ after ^{13}C-lactose ingestion, and of breath radioactivity after ^{14}C-lactose ingestion. Among the blood tests there are the lactose tolerance test, the lactose tolerance test with ethanol, and the milk tolerance test. Lactose maldigestion can also be determined by measuring urinary galactose, at lactose tolerance test with ethanol, either quantitatively or qualitatively, using an enzymatic test strip.

Less reliable stool tests include stool pH, faecal reducing substances, and paper chromatography for the measurement of sugar in the faeces, which are not recommended for research purposes. The widely used breath hydrogen test is a fairly reliable method for the diagnosis of lactose maldigestion, and the amount of hydrogen excreted correlates with maldigested lactose.

The use of laboratory methods for diagnosing lactose intolerance (i.e. symptomatic lactose maldigestion) is not enough. During a lactose tolerance test, the development of gastrointestinal symptoms must always be recorded alongside the laboratory results. A subject with hypolactasia who suffers no gastrointestinal symptoms during the test cannot be regarded as lactose intolerant.

We evaluated (1) the diagnosis situations as regards adults in Finnish health care centres in order to standardise the details of the lactose tolerance tests used. Of all the centres, 97% used lactose tolerance tests for diagnosing lactose intolerance. The cut-off values for measuring the blood glucose elevation varied greatly, from 0.5 mmol/l to 1.7 mmol/l, which shows that no commonly accepted criterion for diagnosing hypolactasia exists.

The correlation between hypolactasia and gastrointestinal symptoms differs when different diagnostic variables are used. Our results (2) showed the correlation between blood glucose concentration and gastrointestinal symptoms to be fair, the concentration of expired breath hydrogen and symptoms to be moderate and the concentration of urinary galactose and symptoms to be good. In practice, this means that if, during the tolerance test, only the blood glucose concentration is measured, the number of false diagnoses is likely to be high.

We have noticed that the intensity of the gastrointestinal symptoms may increase from 1 h right up to 6 h after the beginning of the test (3,4). According to the questionnaire study, in 72% of the health care centres symptoms are only recorded during the actual laboratory tests (40–60 min). The introduction of a written questionnaire on which patients can mark symptoms and their intensity during the 4–6 h following the tolerance test itself would be a clear improvement.

Factors influencing the symptoms

The amount of lactose?

The amount of lactose (50 g) used in the lactose tolerance test is unnecessarily high for diagnosing lactose intolerance, that is, for observing the gastrointestinal symptoms caused by unabsorbed lactose. This dose causes symptoms even to those hypolactasia subjects who can tolerate small daily doses of lactose (5). We (2) have noticed that about 20% of "healthy" subjects who can digest normal doses of lactose suffer gastrointestinal symptoms after this 50 g dose of lactose as well as after other disaccharides. By measuring exhaled breath hypolactasia can be diagnosed with smaller amounts of lactose.

Some maldigesters believe that lactose, even in quantities <1 g, produces symptoms. We examined whether small doses of lactose-induced symptoms in lactose maldigesters and lactose digesters in a randomised, crossover, double-blind design (5). The test doses were 200 ml fat-free, lactose-free milk to which 0, 0.5 1.5 and 7 g lactose was added. Every third day on a lactose-free diet, after and overnight fast, the subjects drank one of the test milks in random order and registered the occurrence and severity of gastrointestinal symptoms in the next 12 h. There was no difference in the mean severity of the reported symptoms between the test milks and the lactose-free milk in the group of lactose maldigesters, of whom one-third did not experience any symptoms from any test doses. The same proportion (64%) of the maldigesters experienced symptoms after both the lactose-free milk and the milk with 7 g lactose. However, the symptoms occurred inconsistently with the different test doses in 59% of the

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maldigesters. Thus, it can be concluded that the gastrointestinal symptoms in most lactose maldigesters are not induced by lactose when small amounts (0.5–7.0 g) of lactose are included in the diet.

Gastric emptying rate

It has been suggested that delayed gastric emptying improves lactose digestion and therefore tolerance. In several studies, lactose has been better digested and the symptoms of lactose intolerance have diminished when lactose has been consumed in milk instead of water, in chocolate milk instead of plain milk or with a meal or dietary fibre. Rapid transit is thought to reduce substrate mucosal contact time and to deliver larger quantities of unabsorbed carbohydrate to the colon more quickly. Conversely, prolonged gastric emptying and intestinal transit could theoretically have the opposite effects.

In our studies, we found that the propantheline-induced prolongation of gastric emptying improved tolerance to lactose, as measured by diminished gastrointestinal symptoms and reduced breath hydrogen concentration (6). On the basis of these findings, factors (dietary and/or pharmalogical) which retard gastric emptying can be recommended for lactose-intolerant subjects along with the recommendation to take lactose together with other foods.

Composition of milk

It has been suggested that full-fat milk causes fewer symptoms in lactose maldigesters than lactose-free milk, because fat slows down the rate of gastric emptying, increases the jejunal transit time, and improves the absorption of carbohydrates. The results of previous studies were contradictory and the difference in the fat content has not been large. We hypothesised that a larger difference than that between fat-free and full-fat milk might be needed before the effect on lactose tolerance manifests itself. In our study, lactose maldigesters ingested milks containing 0 g or 16 g fat/portion twice a day for two days. Both milks contained 10 g lactose/portion. According to the symptom records, there was no difference in the tolerance between the high-fat and the fat-free milks.

Sensitivity to non-absorbable carbohydrates?

Because the symptoms caused by non-absorbable carbohydrates resemble those of lactose in lactose maldigesters with lactose intolerance, symptoms caused by other carbohydrates are often mistakenly considered to be caused by lactose. We examined whether the symptoms caused by large quantities of carbohydrates are more severe in lactose maldigesters with lactose intolerance than in control lactose digesters or in lactose digesters who report milk to be the cause of their gastrointestinal symptoms (pseudolactose intolerant subjects).

The subjects were given either 50 g lactose, 50 g sucrose, 25 g lactulose, or 25 g fructooligosaccharides. After carbohydrate ingestion, urine was collected and the breath-hydrogen concentration was measured every 20 min for 1 h and subjective gastrointestinal symptoms were monitored for 8 h with a questionnaire.

When the lactulose and fructooligosaccharides were ingested, the lactose maldigesters with lactose intolerance and the pseudolactose intolerant subjects, reported more symptoms than did the control lactose digesters. Sucrose caused more symptoms in the subjects with lactose intolerance than in the control lactose digesters.

The data from the completed questionnaires supported the results showing that the pseudolactose intolerant subjects and, to some extent the lactose maldigesters with lactose intolerance, experienced symptoms from certain foods other than milk products more often than did the control lactose digesters.

The results suggest that in subjects with pseudolactose intolerant subjects, the cause of symptoms may be ingestible carbohydrates rather than lactose and that symptoms from all four carbohydrates are more severe in the lactose maldigesters with lactose intolerance than in the control lactose digesters. The reason for this intestinal sensitivity is not known.

Diagnostic approach

Secondary hypolactasia and pseudohypolactasia

We combined our data from 4 different studies. In 68 subjects (mean age: 35 y; range: 18–65 y; 60 females and 10 males) who participated in our blinded crossover studies (2,6,7,8), in order to demonstrate how often subjects who consider themselves to be lactose intolerant really are, when a careful diagnosis is performed (9).

We used the three most commonly used lactose tolerance tests in these subjects. The diagnostic variables were as follows: increased blood glucose ≤1.1 mmol/l, increased excretion of breath hydrogen ≥ 20 ppm and excreted urinary galactose ≤20 mg/3 h. Thirty-one subjects had previously received a diagnosis of lactose intolerance by a health care professional and the remaining 37 subjects were self-diagnosed. Using our gold standard of at least two of the diagnostic variables being positive after ingestion of 50 g lactose in 250 or 300 ml water after an overnight fast (10 h), we found only half of the 31 subjects with a previous diagnosis of lactose tolerance and 40% of the 37 self-diagnosed subjects to be lactose maldigesters (Figure 1).

Surprisingly, one-third of the 29 subjects diagnosed by us as lactose maldigesters had no clinically significant gastrointestinal symptoms for 3 h after ingesting 50 g lactose. At the same time, one-fourth of the 39 lactose digesters experienced clinically significant gastrointestinal symptoms after ingesting the same amount of lactose. Flatulence was the most severe symp-

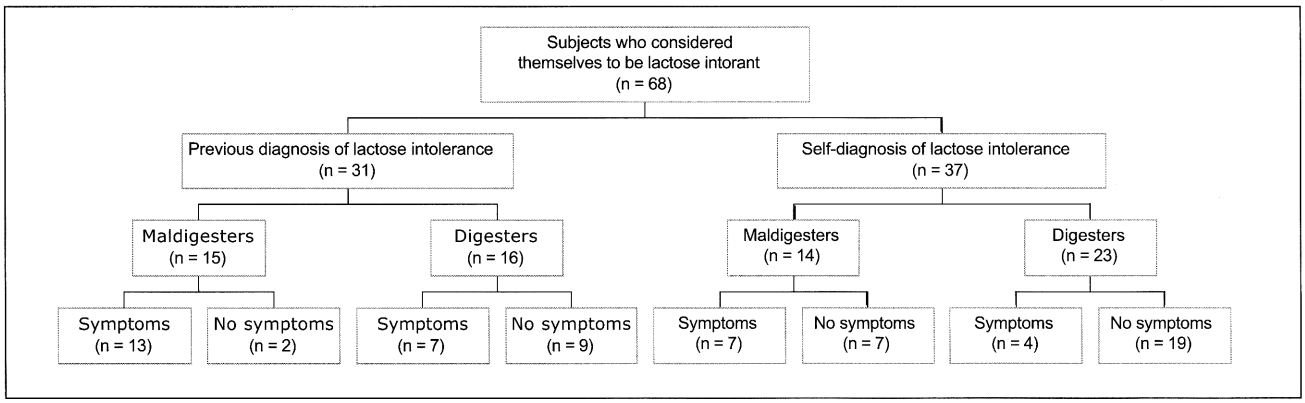

Figure 1. Distribution of subjects with a previous diagnosis of lactose maldigestion and those self-diagnosed as lactose intolerant according to symptoms and laboratory findings of 50 g lactose in a blinded crossover study design in our laboratory. Modified from Peuhkuri et al. 2000 (9).

tom in the maldigesters and abdominal bloating was the most severe symptom in the symptomatic digesters. In both of these groups, the severity of the other symptoms was roughly the same. Clearly, there is a danger that those lactose digesters who experienced symptoms could receive an incorrect diagnosis of lactose intolerance. Thus is essential that the diagnostic tests be conducted carefully.

It is obvious that secondary-lactose intolerance due to epithelial damage (secondary hypolactasia) is common. Therefore, the diagnosis of lactose intolerance needs to be made with carefully controlled clinical lactose tolerance tests, preferably more than one. In cases in which values are borderline, a repeat test should be conducted, preferably with the use of a different diagnostic method after a period of time.

Irritable bowel syndrome

It has been suggested that the symptoms of irritable bowel syndrome (IBS) may be wrongly attributed to lactose intolerance. We examined (10) the relations among IBS, demographic factors, living habits, and lactose intolerance. On the basis of a lactose tolerance test with ethanol, 101 of the 427 healthy subjects studied were lactose maldigesters and 326 were lactose digesters. IBS was diagnosed according to the Rome criteria. The use of dairy products and symptoms experienced after their consumption were recorded. IBS was found in 15% of both the lactose maldigesters and lactose digesters. One-third of the subjects reported intolerance to dairy products containing ≤20 g lactose. About half of this third were lactose maldigesters and about half were lactose digesters.

Of the subjects with IBS, the percentage of lactose maldigesters was the same as in the whole study group (24%) but the number who reported lactose intolerance was higher (60% compared with 27%). We showed a strong relation between subjective lactose intolerance, IBS, the experience of abdominal pain in childhood, and female sex. Whether these association are of psychological or physiological origin, remains to be determined.

Treatment of lactose intolerance

Unlike in allergies, consumption of the substrate-causing symptoms is not harmful in lactose intolerance, but it may be very annoying. There are several options to solve the problem (Table 1).

The treatment chosen should depend on the severity of the intolerance, and often it is affected by the options available. Avoidance of dairy products is seldom necessary, as most lactose-intolerant individuals are able to consume at least some grams of lactose daily. In addition, fermented dairy products like yoghurt are very well tolerated even in larger quantities, and most types of matured cheese do not contain any lactose. Table 2 presents the average content of lactose in dairy products.

Lactose is the main carbohydrate of milk and many dairy products thus contain lactose. But there are also dairy products with naturally low lactose content, e.g. processed soft cheeses and butter. Hard and semihard cheeses are virtually lactose-free. When milk is fermented with lactic acid bacteria, lactose is metabolised to lactic acid. Therefore, all fermented dairy products have lower lactose content than fresh milk.

In hydrolysed products, lactose is hydrolysed to glucose and galactose by an enzymatic method. The content of lactose is usually guaranteed to be less than 20% of that in normal milk. This means that the content of lactose is lower than 1 g in 100 g of the finished product. It is such a low concentration that most of the lactose-intolerant people tolerate these products without any problems.

A chromatographic separation method has been developed (11,12) in order to remove lactose from milk. This lactose-free (and carbohydrate-free) milk gives totally new possibilities for the development of new type of dairy products.

Pharmaceutical preparations of fungal or yeast-derived ß-galactosidase have been developed for the treatment of lactose maldigestion. There is evidence that these preparations increase lactose digestion and alleviate symptoms, but different preparations seem to vary in their effectiveness, and they do not help all subjects.

As milk and milk products are important sources of many nutrients, such as protein, calcium and riboflavin, avoidance of dairy products is not advised without good reason.

Table 1. Options for treatment of lactose intolerance.

Solution	Possible effects
Less dairy products	Poorer diet, deficiency of calcium
Low-lactose products	
fermented	-
lactose hydrolysed	Sweet taste in some products
Lactose-free products	
matured cheese	-
chromatographically separated lactose	Products not yet widely available
Lactase preparations	
added in the product	Sweet taste in some products, expensive
consumed with the product	Not efficient in all individuals, expensive

Table 2. Average content of lactose in dairy products.

	Lactose g / 100 g	Serving size	Lactose g / serving
Ice cream	6	50 – 100 g	3 – 6
Fresh milk	4.8	0.2 l	9.6
Natural yoghurt	3.5	0.2 l	7.0
Cottage cheese	1.6	50 – 100 g	0.8 – 1.6
Butter	0.7	5 – 10 g	0.04 – 0.07
Hard cheese	0		0

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