

Lactose intolerance and milk consumption

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Summary

The disaccharide lactose is one of the main components of milk. During the digestion, it is hydrolysed by the enzyme β -galactosidase into glucose and galactose. With the exception of the Caucasian populations the lactase activity decreases in most people in the age of weaning. After the ingestion of large amounts of lactose, symptoms as bloating, flatulence, abdominal pain and diarrhea can occur due to the lactose reaching the large intestine. This phenomenon is called lactose intolerance or lactose maldigestion. But also in Caucasian populations there are some people who suffer from it. In the past, such populations have used this phenomenon, after weaning, to discourage the consumption of milk. However, nowadays it is recognised that lactose maldigesters can tolerate one cup of milk or two cups of milk a day, when taken over the day with meals. They can also consume cheese that contains no or only small amounts of lactose. Studies performed during the last 15 years have shown that yogurt is very well tolerated by lactose maldigesters. This is attributed to the presence of living lactic acid bacteria in fermented dairy products and to the lactase present in these products.

Key words: lactose intolerance, lactose maldigestion, milk, yogurt, cheese

Lactose is the predominant carbohydrate in milk of mammals. It is a disaccharide consisting of the monosaccharides glucose and galactose by a 1,4 β -glycosidic bond. After consumption, lactose is broken down in the human small intestine by the enzyme β -galactosidase (β -D-galactosido-galactohydrolase, EC 3.2.1.23), also called lactase. The resulting monosaccharide are absorbed into the bloodstream.

In human being, intestinal lactase activity changes during life. After reaching a maximum at term of pregnancy, it remains at a high level during infancy and early childhood. Thereafter the intestinal lactase activity gradually declines. In a minority of the world's population, mostly persons of European origin, high levels of this intestinal enzyme persist into adulthood. These persons are able to readily digest large amounts of lactose. This phenomenon is called lactase persistency and is genetically determined. However, the majority of the world's population have a reduced lactase activity in the small intestine. In this case undigested lactose reaches the large intestine and, when the consumed amount of lactose is greater than the remaining lactase activity, they have difficulties in

digesting it. The enteric bacteria in the large intestine ferment the lactose and produce lactic acid, short chain fatty acids, carbon dioxide, hydrogen gas as well as methane. The formation of these products can result in a variety of symptoms such as flatulence, abdominal pain, diarrhea, and nausea (Sieber, et al., 1997.).

Definition of lactose intolerance and lactose maldigestion

As there are different terms which exist, it is necessary to make necessary differentiation. According to Scrimshaw and Murray (1988.), lactose intolerance is an inability to tolerate a standard or test dose of lactose without developing diagnostic biochemical changes with or without clinical signs and symptoms of bloating, flatulence, abdominal pain and diarrhea. It is also the experience of symptoms of gastrointestinal discomfort after lactose consumption. Lactose maldigestion means the insufficient digestion of lactose due to a low intestinal lactase activity in the brush border membrane of the mucosa. The diagnosis can be made by different lactose tolerance tests. Lactose malabsorption is an unprecise term because lactose is not absorbed. However, milk intolerance is a more general term and can be due to lactose intolerance, but also to milk allergy or just to a negative psychological attitude towards milk.

Diagnosis of lactose maldigestion

Several methods are available to diagnose hypolactasia or lactose maldigestion and a comprehensive presentation of this topic is given by Arola (1994.):

1. assessment of clinical origin and symptoms after lactose ingestion and
2. laboratory methods.

With the first method, a test dose of 50 g lactose is given and the passage of one or more liquid stools is reported (lactose loading) or the symptoms (loose stools, gas, bloating and cramps) are recorded and graded. Both tests are non-invasive and somewhat unreliable. The laboratory methods can be divided in different groups such as invasive methods (assay of mucosal disaccharidases, intestinal perfusion studies), abdominal X-ray investigation, stool tests (measuring of stool pH or fecal radioactivity after ^{14}C -lactose administration) and lactose intolerance tests. The latter are divided in breath (breath hydrogen test after lactose ingestion, breath radioactivity after ^{14}C -lactose or breath $^{13}\text{CO}_2$ after ^{13}C -lactose ingestion), blood (lactose tolerance test, milk tolerance test, complete or simple lactose test with ethanol) and urine tests (lactose tolerance test with ethanol based on urinary galactose determination after lactose ingestion or with or without ethanol with qualitative urinary galactose detection with a test strip or with 3-methylactose or based on the determination of total urinary galactose or galactose/creatinine ration, lactose to lactulose ratio).

The lactose tolerance test was used for many years. It is based on the measurement of the increase in blood glucose at intervals of 15 to 30 min over 30 min to 2 h after an oral standard dose of 50 g lactose. Today, the most used method is the breath hydrogen determination after ingestion of physiologic dose of 12.5 g or of the usual tolerance test dose of 50 g. Hydrogen from expired air samples which are taken at zero and at intervals of 15 to 60 min for 2 to 8 hr is measured. Usually a cut-off point of 20 ppm hydrogen is used.

Prevalence of hypolactasia

The adult-type hypolactasia considerably prevails between different races and populations. The results of numerous studies, reviewed by Sahi (1994.), showed that at the international level the majority of adults has a low lactase activity. This phenomenon is especially met, after weaning, in the Asian and African populations (exceptions are cattle-raising population, for example nomadic Fulani in Nigeria and Tuaregs in Niger), in the American Indians, Eskimos and the black of America. However, in Europe, North America and Australia, the prevalence of hypolactasia is typically less than 30 % of adults and only in a few cases more than 60 %. To explain this, two hypothesis have been made: in the first one, the adaptive or induction hypothesis, - there is little proofs for human beings - it is said that lactase activity is regulated by the lactose quantity contained in food. On the contrary, the genetical hypothesis, based on family studies, says that in the Caucasian population the persistent lactase activity is inherited in an autosomal-dominant way.

In Slovenia, Micetic-Turk (1982.) studied a group of children aged from 7 weeks to 15 years of age using a normal lactose tolerance test and found a prevalence of 33 %. Using a breath hydrogen test, the prevalence of hypolactasia in 8 to 15 year adolescent was 24 % and in 14 to 15 year old adolescent 26 % (Micetic-Turk, unpublished results, cited after 4) and is similar to that found in Eastern Austria (25 %) (Rosenkranz et al., 1982.).

Occurrence of lactose in milk and dairy products

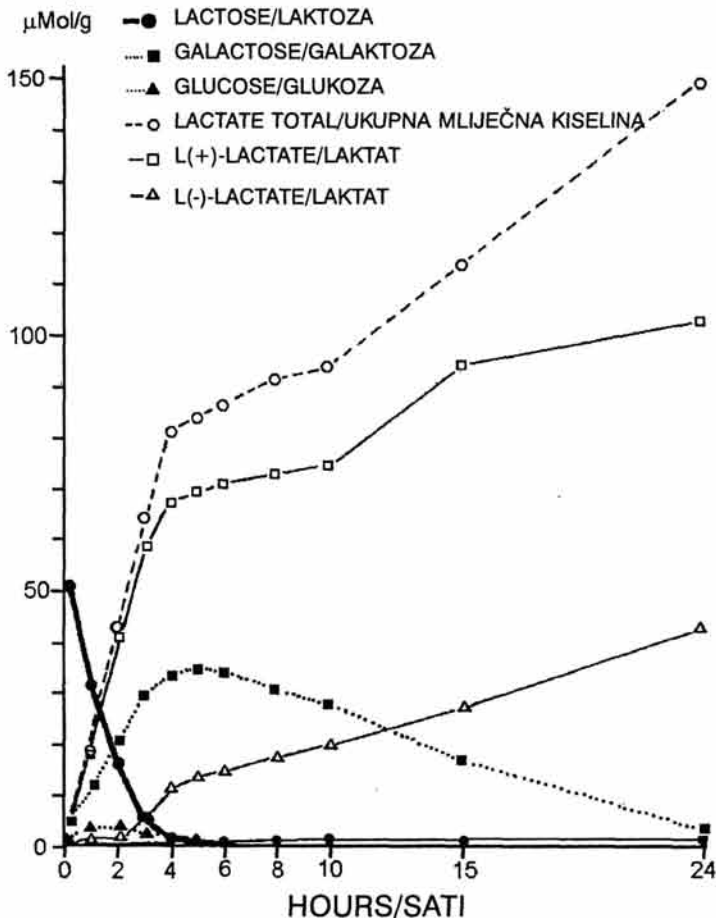
Cow's milk normally has a lactose concentration of 4.6 to 4.7 g/dl (Sieber, et al., 1999.). The milk of the following mammals contains: human being 7.0, sheep 4.8, mare 6.2, goat 4.1 g of lactose/dl. Furthermore, the milk of the California sea lion does not contain lactose, while 10.2 g of lactose/dl had been detected in the milk of the green monkey (*Cercopithecus sabeus*) (Jenness and Sloan, 1970.). During the processing of cow milk, the lactose goes into the product. In fermented dairy products, lactose is broken down by lactic acid bacteria. In natural yogurt, the lactose concentration is reduced by 1/3 compared to milk (3.4 g/100 g) (Sieber et al., 1996.). But in yogurt manufacture, it is pos-

sible to increase the dry matter by adding milk powder or by concentrating the milk. Doing so, the lactose concentration of yogurt can vary: yogurt with fruit or flavour between 2.9 and 4.2 g/100 g. In other dairy products such as cream (Sieber et al., 1996.), butter (Sieber et al., 1998.), quark and cottage cheese (Sieber et al., 1999.), the lactose concentration is also reduced compared to milk (g/100 g): full cream 3.1, half cream pasteurised 3.3 and UHT 3.7, coffee cream 3.8, butter 0.6, energy-reduced butter 1.1, fried butter 0, cream quark 3.2, skim quark 3.5 and cottage cheese 2.2.

In former times when the carbohydrate content of food was calculated from dry matter minus protein, fat and ashes, the measured values for cheese

Figure 1: Degradation of lactose in Emmental cheese during the first 24 hours (from 16, modified)

Slika 1: Razgradnja laktoze u Emmentaler siru tijekom prvih 24 sata (modifikacija lit. 16)



were up to 4.7 g of lactose/100 g (Scrimshaw and Murray, 1988.; Högl et al., 1969.; Souci et al., 1979.). Still in the release 12 of the US Department of Agriculture Food Composition Data, carbohydrate content of cheese is calculated by difference (U.S. Department..., 1998.). Studies by Steffen (Steffen, 1975.) have shown that, in hard cheese and semi-hard cheese, lactose is completely broken down into glucose and galactose during the first 5 to 10 hours of cheese ripening. Both are then transformed into lactic acid (figure 1). Further studies on the ripening of hard cheese (Gruyère, Sbrinz) and semi-hard cheese (Appenzell, Tilsit) have confirmed these observations (Sieber et al., 1988.; Sieber et al., 1994.; Schär et al., 1992.; Sollberger et al., 1991.; Steffen et al., 1992.; Steffen et al., 1993.; Steffen et al., 1993.). The results of researches done in our laboratory showed that in semi-hard and soft cheese almost all lactose contained is degraded. In only 6 from 62 cheese samples the lactose was detected: two Brie samples (11 and 85 mg/100 g), one Raclette sample from pasteurised milk (10 mg/100 g), one Tomme sample (10 mg/100 g) and two Vacherin Mont d'Or samples (50 and 80 mg/100 g) (Sieber et al., 1994.).

Tolerance of lactose in water solution

The quantity of 50 g of lactose, used for the lactose tolerance test, induces symptoms of intolerance in most lactose maldigesters. According to Hertzler

Table 1: Breath hydrogen production and symptom responses to four doses of lactose compared to zero-lactose control (n=13) (Hertzler et al., 1996.)

Tablica 1: Količina nastalog vodika u dahu i simptomi uzrokovani dodatkom 4 različite doze laktoze u usporedbi s kontrolnim uzorkom bez laktoze (n=13) (Hertzler i sur., 1996.)

Treatment Doza	Hydrogen production Količina nastalog vodika		Flatus Vjetar		Abdominal pain Bol u trbuhu	Diarrhea Diareja
	total ¹ ukupno ppm	peak ¹ max. ppm	Frequency rank ^{1,2} Učestalost	Rating rank ^{1,2} Ocjena		
0	77.1±14.0 ^a	12.1±2.4 ^a	2.7±0.6 ^a	2.7±0.3 ^{ab}	2.4±0.3 ^a	2.9±0.2 ^a
2	55.5±11.4 ^a	7.5±2.1 ^b	2.5±0.4 ^a	3.0±0.3 ^b	2.5±0.2 ^a	2.9±0.2 ^a
6	145.2±26.4 ^b	21.1±5.1 ^a	2.4±0.3 ^a	1.9±0.2 ^a	2.4±0.2 ^a	2.7±0.2 ^a
12	291.9±40.6 ^c	49.0±9.4 ^c	3.2±0.4 ^a	3.2±0.4 ^b	3.8±0.3 ^b	2.5±0.2 ^a
20	488.2±64.4 ^d	82.2±18.7 ^c	4.3±0.3 ^b	4.2±0.3 ^c	3.9±0.3 ^b	3.5±0.3 ^a

¹ Values in a column that do not share the same letter are significantly different (p<0.05)

¹ Vrijednosti u stupcu koje nisu označene istim slovom značajno se razlikuju (p<0.05)

² Treatments were ranked 1 (least symptoms) through 5 (most symptoms).

² Primjenjene doze su ocijenjene od 1 (najmanje izraženi simptomi) do 5 (većina prisutnih simptoma).

et al. (1996.), the minimum dose of lactose, required to cause notable lactose maldigestion and symptom response, have not been established. These authors fed 0, 2, 6, 12 and 20 g lactose in 240 ml aqueous solution (double-blind, randomised protocol) to 13 healthy free-living lactose maldigesters and measured breath hydrogen production and symptom responses to each challenge dose. Breath hydrogen production over the 8-hour period was negligible after consumption of the 0- and 2-g lactose doses (table 1) while increased after consumption of the other three doses. However, after the 6-g challenge, hydrogen production remained near fasting levels and increased at the 4-hour point compared with the 0-g and 2-g lactose doses. Intensity of flatus frequency and abdominal pain as well as severity of diarrhea were similar when the dose of lactose was 0, 2 or 6 g. These authors stated that, up to 6 g dose, lactose was tolerated, even though maldigestion could be measured at the 6-g dose.

Tolerance of small amounts of milk

It has been demonstrated that lactose-intolerant persons digest the same quantity of lactose in a different way if it is in water solution or in milk. A comparison between the same amount of lactose (18 g) in water and in milk showed a similar rise in breath hydrogen excretion. However, the rise after ingestion of milk occurred later than after the aqueous lactose solution. The areas under the curve were not statistically different (12480 ± 1680 and 17040 ± 4320 ppm/8 hours after milk and lactose ingestion (Dewit et al., 1988.).

Several studies examined whether small doses of lactose can be tolerated by lactose maldigesters. In a randomised, crossover, double-blind study, 39 lactose maldigesters and 15 lactose digesters received 200 ml fat-free, lactose-free milk to which 0, 0.5, 1.5, and 7 g lactose was added. The lactose maldigesters reported significantly more occasions of abdominal bloating and abdominal pain than the digesters (figure 2). In the group of lactose maldigesters, the mean severity of the reported symptoms between the test milks and the lactose-free milk was not different (Vesa et al., 1996.). In a further double-blind study (Suarez et al., 1995.), 21 persons who believed they were severely lactose-intolerant received 240 ml of regular milk (= 12.1 g of lactose) or lactose-hydrolysed milk for two one-week periods and rated the occurrence and severity of gastrointestinal symptoms experienced during the 24-hour period after each test meal. Reported symptoms were minimal (table 2). According to these authors, lactose-intolerant subjects do not need lactose-digestive aids when lactose intake is limited to the equivalent of 240 ml of milk a day. Furthermore, they investigated in a double-blind study whether lactose-intolerant persons are able to tolerate the daily ingestion of two cups of milk (Suarez et al., 1997.). 19 persons self-described as markedly lactose-intolerant and 13 persons who denied lactose intolerance ingested 240 ml of regular or lactose-hydrolysed milk

Figure 2: Percentage of lactose maldigesters (n=39) and lactose digesters (n=15) who experienced symptoms during the test day after ingestion of 0, 0.5, 1.5 and 7.0 g of lactose (Vesa et al., 1996.)

a = significantly different from lactose-free milk (p < 0.05)

Slika 2: Postotak osoba osjetljiv na laktozu (n=39) i osoba koje apsorbiraju laktozu (n=15) koje su pokazale zdravstvene simptome tijekom testa uzimanja 0, 0.5, 1.5, i 7.0 g laktoze (Vesa i sur., 1996.)

a = Značajno različito od mlijeka oslobođenog od laktoze (p < 0.05)

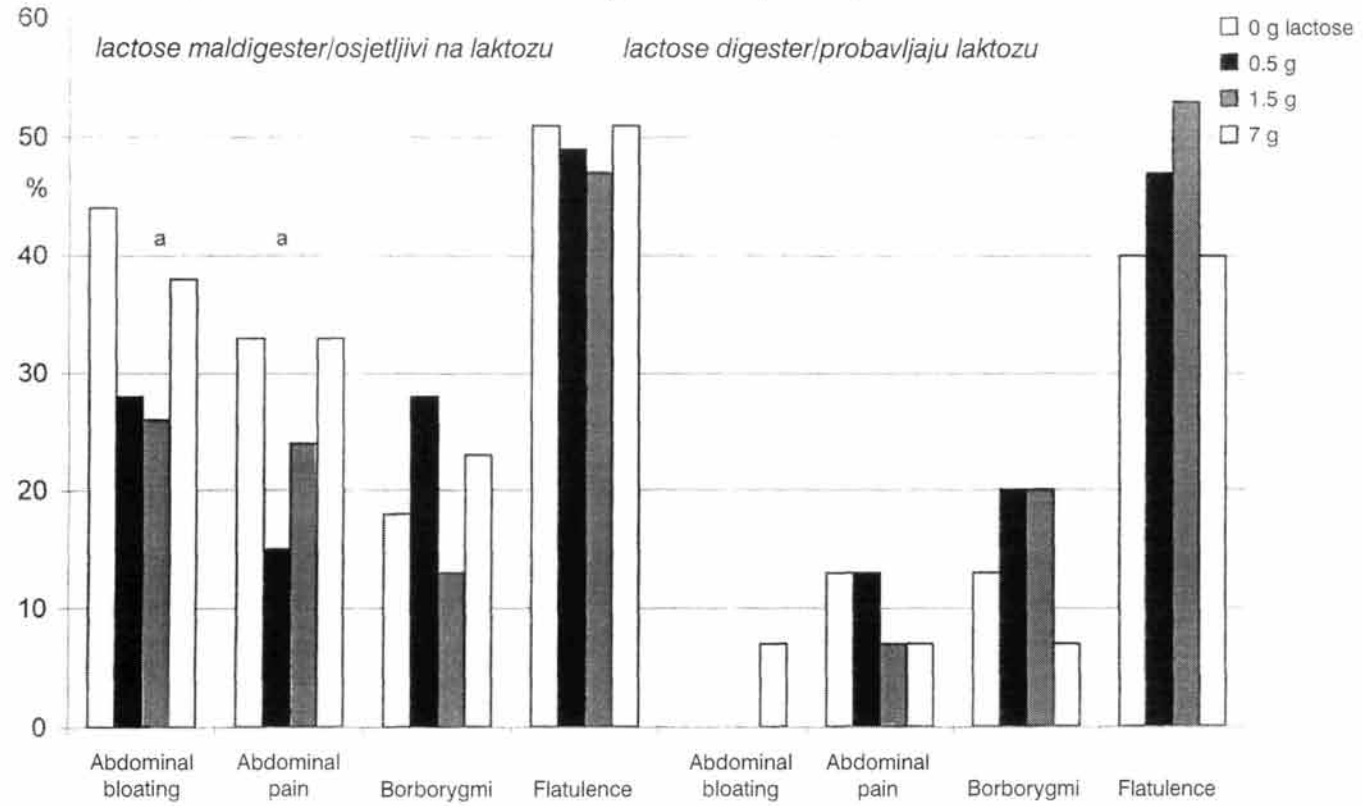


Table 2: Gastrointestinal symptoms and frequency of flatus in 30 self-reported lactose-intolerant persons after drinking 240 ml regular milk or lactose-hydrolysed milk (n=30) (Suarez et al., 1995.)

Tablica 2: Gastrointestinalni simptomi i učestalost vjetrova kod 30 ispitanih osoba, koje sebe smatraju osjetljivim na laktozu, nakon konzumacije 240 mL običnog mlijeka ili mlijeka s hidroliziranom laktozom (n=30) (Suarez i sur., 1995.)

Symptoms Simptomi	Regular milk Obično mlijeko		Lactose-hydrolysed milk Mlijeko s hidroliziranom laktozom	
	mean prosjeak	SD SD	mean prosjeak	SD SD
Lactose-maldigestion group (n=21) Grupa ispitanika osjetljivih na laktozu (n=21)				
Bloating ¹ /Naduvanost ¹	0.6	0.1	0.5	0.1
Abdominal pain ¹ /Bol u trbuhu ¹	0.4	0.1	0.3	0.1
Diarrhea (episodes/day)/Učestalost diareje po danu	0.1	0.0	0.3	0.1
Flatus/Vjetrovi				
Perceived severity ¹ Opaženi žestoki simptomi ¹	1.1	0.1	0.0	0.1
Frequency (episodes/day) Učestalost/danu	10.1	1.5	7.6	1.2
Lactose-digestion group (n=9) Grupa ispitanika sa sposobnošću apsorpcije laktoze (n=9)				
Bloating ¹ /Naduvanost ¹	0.6	0.2	0.5	0.2
Abdominal pain ¹ /Bol u trbuhu ¹	0.6	0.2	0.4	0.2
Diarrhea (episodes/day)/Učestalost diareje po danu	0.3	0.2	0.2	0.1
Flatus/Vjetrovi				
Perceived severity ¹ Opaženi žestoki simptomi ¹	0.9	0.2	1.2	0.2
Frequency (episodes/day) Učestalost/danu	11.8	2.3	8.4	1.9

¹Ranking of symptoms: 0 no, 1 trivial, 2 mild, 3 moderate, 4 strong and 5 severe symptoms.

¹Ocjenjivanje simptoma: 0 - bez simptoma, 1 - neznatni, 2 - blagi, 3 - umjereni, 4 - izraženi i 5 - žestoki simptomi

with breakfast and dinner for 7 days. Gastrointestinal symptoms reported by both groups were minimal and the severity of abdominal pain, diarrhea, and bloating was not significantly different. These authors concluded that lactose-intolerant persons are able to tolerate the daily ingestion of two cups of milk with breakfast and dinner. Other randomised, double-blind studies confirmed the observation that almost everyone could tolerate up to 12 grams of lactose a

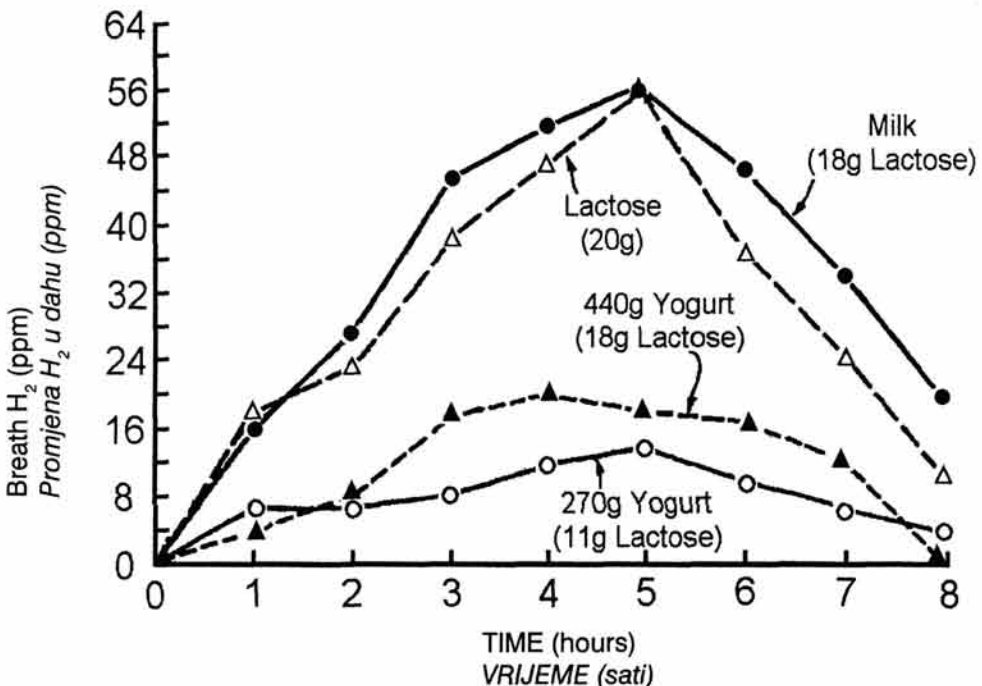
day, which corresponds to a cup of milk, without experiencing any symptoms (Haverberg et al., 1980.; Newcomer, et al., 1978.; Rorick and Scrimshaw, 1979.; Unger and Scrimshaw, 1981.).

Other dietary approaches

In spite of the remaining lactose, lactose intolerant persons are able to digest yogurt (see also 1). This fact was demonstrated in a study by Kolars et al. (1984.) using a H_2 breath test. He observed lower breath hydrogen concentration after ingestion of yogurt than milk or lactose in water (figure 3). Studies by Gilliland and Kim (1984.), Savaiano et al. (1984.), Martini et al. (1987., 1991.), McDonough et al. (1987.), Dewit et al. (1988.), Rosado et al. (1992.) and Murao et al. (1993.) showed the favourable effect of yogurt compared to milk. By heating yogurt, lactase activity is reduced by approximately 10-fold (Savaiano et al., 1984.) or is effectively eliminated (McDonough et al., 1984.).

Figure 3: Change in breath hydrogen concentration after ingestion of lactose, milk or yogurt (from 33, modified)

Slika 3: Promjena koncentracije vodika u dahu nakon konzumacije laktoze, mlijeka ili jogurta (modifikacija lit. 33)



Various authors found a statistical significant higher breath hydrogen concentration after the consumption of heated yogurt compared to unheated yogurt (Dewit et al., 1988.; Gilliland and Kim, 1984.; McDonough et al., 1987.; Lerebours et al., 1989.), but let's mention that other authors did not confirm this (Savaiano et al., 1984.; Varela-Moreiras et al., 1992.; Marteau et al., 1990.). The different strains and species of lactic acid bacteria varied in their ability to digest lactose in vivo. 12 healthy lactose-intolerant subjects received low fat milk, yogurt (fermented by using a mixture of *Streptococcus (Str.) thermophilus* and *Lactobacillus (L.) bulgaricus*) and four milks fermented by single strains of *Str. thermophilus*, *L. bulgaricus*, *Bifidobacterium (B.) bifidus* or *L. acidophilus* containing 15 g lactose in 260 to 294 g yogurt or milk. Peak hydrogen excretion after milk consumption was about ninefold higher than it was after yogurt consumption. The response to the four fermented milks varied from marginal improvement with milk fermented by *B. bifidum* to nearly complete lactose digestion with milk fermented by *L. bulgaricus* (Martini et al., 1991.).

It is possible, using an oral enzyme replacement therapy, to increase the reduced lactase activity of lactose-intolerant persons. Commercial lactase, obtained from yeast or fungi and available on the market as caplet, chewable tablet or capsule, is ingested either together with, immediately before or shortly after milk ingestion. Several studies reported the efficiency of this therapy (Rosado et al., 1984.; Solomons et al., 1985.; Moskovitz et al., 1987.; Lami et al., 1988.; Sanders et al., 1990.; Lin et al., 1993.; Corazza et al., 1992.). These results were not supported by Onwulata et al. (1989.).

A further possibility is the use of milk with a reduced lactose content obtained by lactose hydrolysis. This technology was elaborated during the seventies and gives a milk with sweeter taste than regular milk (Mahoney, 1985.). Lactose-hydrolysed milk was given to 6 persons with lactose maldigestion and the effect was followed by H₂-breath test. After 300 ml full cream milk had been administered, the peak change of the H₂-excretion rose to 31±6 ppm, and after the administration of milk whose lactose had been reduced by 50, 80 and 95 %, it rose to 7±6, 5±3 and 8±3 ppm (Brand and Holt, 1991.). Only the consumption of 500 ml of milk whose lactose had been reduced by 50 % exceeded the H₂-breath threshold value of 20 ppm (Monro and Brand, 1991.). After the consumption of full cream milk, 5 persons suffered from at least one of the following symptoms: flatulence, diarrhoea or cramps (with a lactose reduced milk by 50%: one person suffered from the symptoms; and one with lactose reduced milk by 80%). After the consumption of lactose reduced milk by 95%, there were no symptoms (Brand and Holt, 1991.). After the administration of a lactose-hydrolysed milk (400 ml, 2 g lactose/100 ml), Kotz et al. (1994.) have registered a H₂-excretion of 9 ppm.h.

Conclusion

New researches showed that most people with lactose maldigestion can still consume up to two cups of milk a day if taken with meals, one at breakfast and the other at dinner. In fact, drinking milk and eating other lactose-containing dairy foods may actually improve a person's ability to digest lactose. Also yogurt and fermented dairy products can generally be well tolerated by lactose-intolerant persons, and they are valuable foods and a good source of calcium supply for this group (Suarez et al., 1998.). The favourable effect of yogurt and other fermented dairy products has to be attributed mainly to the (-galactosidase possessed by microorganisms of starter cultures as well as to the extended passage rate through the intestine.

NEPODNOŠLJIVOST (INTOLERANCIJA) LAKTOZE I POTROŠNJA MLIJEKA

Sažetak

Disaharid laktoza predstavlja jedan od glavnih sastojaka mlijeka. Tijekom probave hidrolizira se djelovanjem enzima β -galaktozidaze, u glukozu i galaktozu. Aktivnost laktaze smanjuje se kod većine rasa (s izuzetkom Kavkaskе rase) i to nakon perioda dojenja. Unošenjem veće količine laktoze u organizam javljaju se različiti simptomi poput naduvenosti, vjetrova, boli u trbuhu, diareje i dr. Ova pojava naziva se intolerancija (nepodnošljivost) laktoze ili neprobavljivost laktoze, koja se može pojaviti čak i kod dijela Kavkaskе rase. U povijesti se ova pojava koristila da bi se ljudi odbili od konzumiranja mlijeka. Međutim moderna znanost je dokazala da ljudi koji ne podnose laktozu mogu konzumirati jednu do dvije šalice mlijeka dnevno bez značajnijih poteškoća. Ova grupa ljudi također može konzumirati sir koji sadržava malu količinu laktoze ili sir u kojem nema laktoze. Istraživanja tijekom 15 godina su pokazala da takova grupa ljudi vrlo dobro podnosi jogurt, što objašnjava prisutnošću živih bakterija mliječne kiseline i laktaze u fermentiranim mliječnim proizvodima.

Ključne riječi: nepodnošljivost laktoze, osjetljivost na laktozu, mlijeko, jogurt, sir

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