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Lactose intolerance: Biochemistry Perspective

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Abstract: Lactose is disaccharide that found mainly in dairy products derived from mammary glands except in sea lions and walruses due to low milk production. It also contains fatty lactose-free milk. β-galactosyl-1,4 glucose.[1] Lactose is an essential sugar for a newborn. Since there randomized comparative studies.[2,3] They gathered breastfed newborns or receiving lactose-containing milk is compared with newborns fed lactose-free milk, the first group of newborns had higher blood sugar levels, nutrients and amino acids than the second group. Studies in adults have found that 14% of their energy intake comes from dairy products, figures from Europe and North America. while the People's Republic of China and developing countries account for only 4%, but the overall consumption of dairy products in all regions is on an upward trend.[4]

Keywords: Lactose intolerance, Lactase deficiency, Malabsorption

Introduction

There is 5 g of lactose in 100 ml of cow's milk, which is equivalent to 12.5 g of lactose in 250 ml of cow's milk, which is more commonly sold in packaged quantities than 100 ml. Others include yogurt and cheese, which are the second largest fermentation industry after alcohol.[4] Yogurt contains half of the unprocessed lactose. Compared to cheese, cheese has less lactose and sugar content. There is even less lactose available if cooked. Lactose has also been found to be produced in powdered form to be used as a common additive in processed foods to add texture and taste to foods such as: sausage, gravy, margarine, bread. In addition, the content of lactose in various foods is shown in Table 1.

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Table 1 shows the content of lactose in various food products

Food type	Lactose content per 100 grams of food (grams)	Lactose content per 1 serving (grams)
Soft ice cream	6.4	5.7
Full milk	4.7	15
Goat's milk	4.5	13
Latte macchiato	4.3	8.6
Biological yogurt	4.0	9.5
Ready sauces	3.6	4.5
Pudding/ custard	3.6	4.5

The digestion and absorption of lactose occurs in the small intestine. The enzyme lactase is coded from the LCT gene located on the second pair of chromosomes consisting of 17 exons. The lactase-phlorizin hydrolase [3.2.1.23] is found in the brush border of the small intestine and is most abundant in the mid-jejunum covering the epithelium of matured enterocytes and contains two identical 160 kDa extracellular polypeptide chains with alpha-glucosidase and beta-galactosidase activity. Part of this enzyme cleaves sugars into monosaccharides, glucose and galactose. These sugars then enter the enterocyte via sodium-glucose cotransporter 1 (SGLT1), is digested in large quantities and enters the enterocyte via glucose transporter 2 (GLUT2) as well.[5-7]

The definition of a condition of lactose deficiency, depletion, or abnormal absorption of lactose can be categorized as shown in Table 2.

Table 2 shows disease or condition related to lactose intolerance

Disease or condition	Definition
Congenital lactase deficiency	A very rare genetic disorder is a frameshift mutation that leads to an inability to produce the enzyme lactase. The symptoms are often severe immediately after birth.
Lactase non-persistence	Reduced intestinal lactase expression in the first 20 years of life. This phenotype is found worldwide.
Lactase persistence	The persistent expression of intestinal lactase enzyme beyond infancy, the phenotype was found to be more common in western countries.
Lactase deficiency	An inability to digest large amounts of lactose due to low activity of the enzyme lactase in the small intestine.
Lactose malabsorption	Conditions with the passage of lactose into the colon as a result of lactase deficiency or other pathologies.
Primary lactose malabsorption	Abnormal lactose malabsorption caused by lactase non-persistence.

Disease or condition	Definition
Secondary lactose malabsorption	Abnormal absorption of lactose caused by decreased lactase expression is commonly caused by acute enteritis, which can be reversible.
Lactose intolerance	Typical gastrointestinal symptoms such as abdominal pain, flatulence, and diarrhea in people with lactose malabsorption after testing by eating lactose sugar
Functional lactose intolerance	Symptoms of lactose intolerance without lactose malabsorption
Self-reported lactose intolerance	Based on the history of symptoms of lactose intolerance without the diagnosis of lactose intolerance or lactose malabsorption.

Lactose malabsorption and Lactose intolerance

Lactose malabsorption is often a condition that leads to lactose intolerance. However, these two conditions require careful diagnosis as they are confusing, and the cause of the condition must be considered separately. It was found that a small number of patients with lactose malabsorption did not experience any abnormalities after consuming standard dairy products. While some people experience symptoms such as borborygmi (a feeling of shaking in the stomach) and flatulence after consuming lactose-containing products. The onset of disease was also found to be strongly associated with the production of hydrogen gas during the breath test. In addition, the digestible sugar lactose in the small intestine caused osmotic trapping and excessive fermentation[8] times the amount of lactose converted to short-chain fatty acids (SCFA).[5] Diarrhea will occur if the associated lactose content exceeds the capacity of the colonic microbiota due to fermentation or excessive amounts of SCFA in the colon as shown in Figure 1.

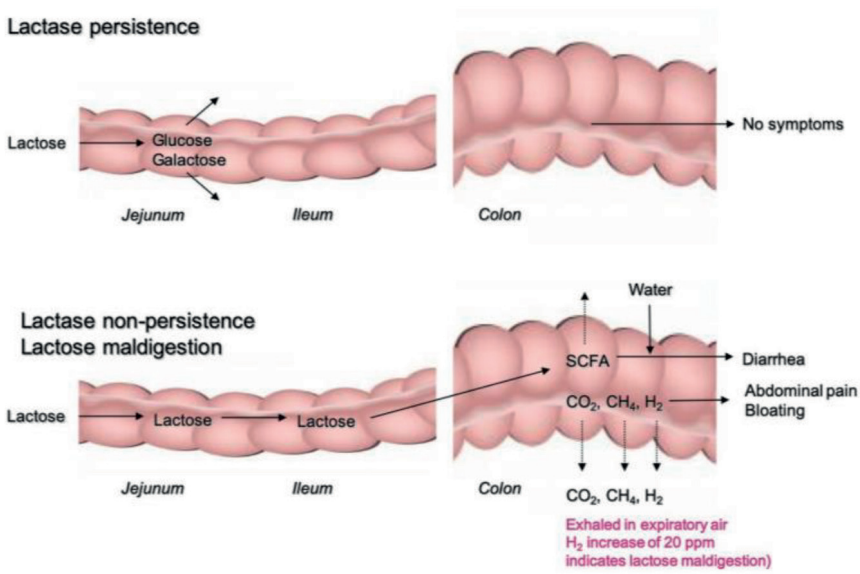

Figure 1 shows the pathophysiology of the enzyme lactase production leading to the fermentation of lactose to short-chain fatty acids, methane, and carbon dioxide. and hydrogen gas, which can lead to diarrhea, abdominal pain, and flatulence.[9]

Fermentation that occurs in the large intestine is caused by the normal state of decreased oxygen in the large intestine. These bacteria transport electrons via NADH to the organic compound resulting from their inability to digest lactose to produce lactose into NAD+, which will have a variety of microbial fermentation forms. But all of these require electron transport receptor generated during the oxidation reaction. Therefore, fermentation requires many organic compounds to accept electrons as mentioned, e.g., short-chain fatty acids, lactic acid, alcohol, etc.[8,10]

There are many factors that can induce lactose intolerance or are classified as lactose intolerance that are multifactorial. It consists of extrinsic factors and intrinsic factors as shown in Figure 2. Examples of extrinsic factors that trigger such as the amount of lactose consumed affects its movement into the small intestine and increases the rate of transport of indigestible lactose into the large intestine. Intrinsic factors that drive the expression of genes that play a role in the production of enzymes responsible for digestion and absorption of diglycerides at the brush border of the small intestine, or the history of abnormal gastrointestinal anatomy. including abnormal intestinal microbiota.[10,11]

Signs and symptoms of lactose intolerance usually appear 30 minutes to 1 to 2 hours after eating foods containing lactose, such as dairy products. The severity of symptoms depends on the amount of lactose consumed and the severity of the disease as mentioned above. The symptoms that can occur include diarrhea, flatulence, abdominal pain, nausea, vomiting, a lot of wind in the stomach, or there may be more than usual burping.[12]

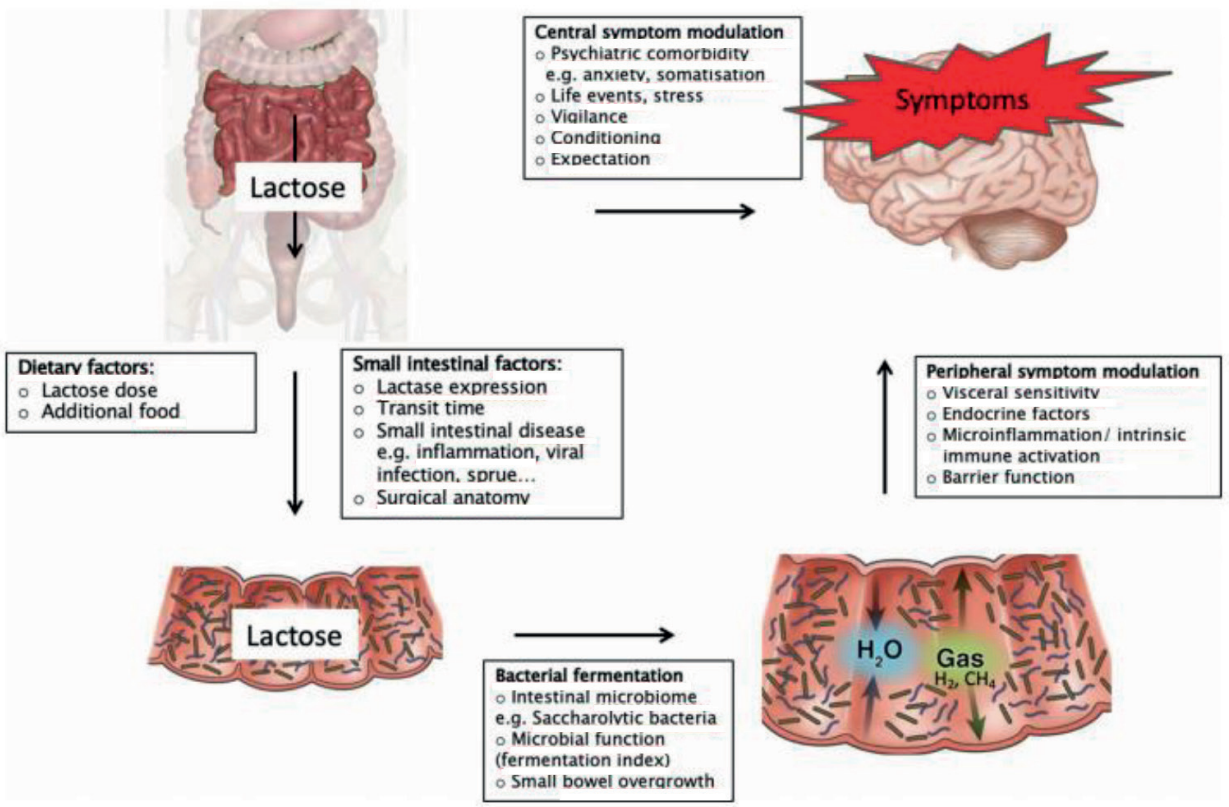

Figure 2 shows the factors inducing lactose intolerance and the pathophysiology

Secondary Lactose Intolerance

Certain conditions or environmental conditions can trigger lactase enzyme deficiency. Rotavirus infection, which is a pathology on the epithelium of the small intestine that is common in children under 5 years of age.[13] The rotavirus can invade the cells of the mature small intestinal epithelium, meaning that the cells are already able to produce the enzyme lactase fully and detachment of the villi, causing villi atrophy, thereby inducing crypt cell hyperplasia. In which these cells are not fully developed so they are unable to produce lactase, even if they can produce it in small amounts in addition to rotavirus infection, other conditions can cause secondary lactose intolerance, such as inflammation of the intestinal mucosa caused by bacterial infection. Infants with cow milk protein allergy (CMPA) are another common cause. Others are patients with small bowel resection or stomach surgery, receiving chemotherapy, opportunistic infections in HIV-infected patients. However, if the trigger or underlying condition is treated, lactose intolerance is also resolved.

Investigation in Lactose Intolerance

Although lactose intolerance can be diagnosed by history taking especially nutritional history, eating history, physical examination but there are cases where history taking physical examination still cannot be clearly identified. Therefore, additional diagnostic tests were sent to confirm it.

Genetic testing using Real-time PCR, in which genomic DNA is extracted from a patient's blood or collected from the buccal area. This method is appropriate in areas where there is a high prevalence of genetic predisposition or in epidemiological studies. In Caucasians, the LCT-13910:C/T polymorphism results in persistent lactase and genetic testing can also identify lactase non-persistent syndrome. However, genetic testing is more complex and genetically heterogeneous in patients of African or Asian descent, where genetic testing is currently considered unsuitable in this population. Additionally, genetic testing cannot be used to diagnose secondary lactose intolerance.

Lactase activity by intestinal biopsy can diagnose both primary and secondary lactose malabsorption. Anesthetized endoscopic examination is not an indication of this test. However, it is important to collect biopsies in patches and check for lactase enzyme activity rather than collecting single biopsies because it will provide more accurate results.[14]

The Hydrogen breath test (HBT) measures the excretion of hydrogen in the respiratory tract after a challenge with a standard dose of lactose (20-25 g of lactose).[15, 16] Since hydrogen cannot be produced by mammalian enzymes, hydrogenation can indicate the presence of sugars in contact with bacteria, which indicates lactose malabsorption. The stool acidity test is based on the principle that unabsorbed lactose is fermented by colonic bacteria into lactic acid, which lowers the pH of the stool.

The lactose tolerance assay measures plasma glucose levels at different times: 0, 30, 60 and 120 minutes after consuming 50 g of lactose. But it is inconvenient for the patients because the blood must be collected several times. Capillary measurement with a portable glucose meter is more convenient and less painful for the test subject but may not be as accurate in diagnosis as venous collecting.[17]

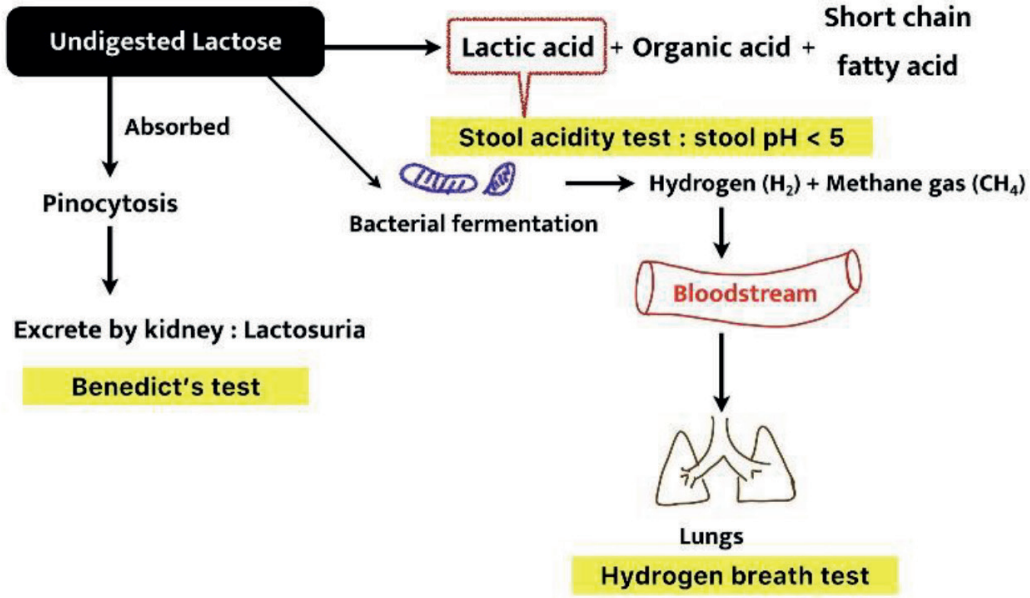

Figure 3 shows the correlation of additional diagnostic tests with the pathophysiology that occurred in patients with lactose intolerance. (Courtesy by Dr. Yutthana Pansuwan)

Management Lactose Intolerance

Management of patients with lactose intolerance aims to maintain the patient's condition and to avoid the risk of long-term malnutrition or malnutrition. There are 4 main points:

(1) Reduce or limit the amount of lactose intake.

(2) Replace lactose with other nutrients.

(3) Substitute enzymes or substances that can digest lactose.

(4) Take calcium and vitamin D supplements.

It is generally recommended that patients follow a diet low in lactose. However, in contrast to the maintenance of this condition, a strict lactose-free diet may not be necessary, as patients with lactose intolerance often tolerate up to 250 ml (12 g of lactose) of milk[16], no symptoms and others when taken with other foods as well the foods high in lactose that should be avoided include: dairy products, soft cheese, butter, ice cream, yogurt, margarine, custard, mashed potatoes, pancakes.

Prebiotics can also be given, which play a role in the management of the colonic microbiota. A randomized, placebo-controlled study in which 85 patients with lactose intolerance was administered orally administered short-chain galactooligosaccharides (GOS, RP-G28), a type of prebiotics, has been found to reduce hydrogen gas production and relieve stomach pain. Additional microbiological examination in the patients studied found that there was an increase in *Bifidobacterium spp*., which is a bacterium capable of producing lactase enzyme.[18,19]

There are now more and more lactose-free dairy products on the market that are considered safe, although some allergic reactions have been reported.[20] These products also reduce lactose crystallization (decrease lactose crystallization) and increase sweetness.[21] Lactase enzymatic treatment in tablet form can both treat lactose digestion leading to reduced hydrogen gas production and alleviate symptoms.[22]

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