LACTOSE INTOLERANCE – A REVIEW

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ABSTRACT
Cow's milk allergy and cow's milk intolerance are often used interchangeably, resulting in confusion in clinical practice and public understanding. Cow's milk intolerance refers to non-allergic, non-immunological reactions to cow's milk such as disorders of digestion, absorption or metabolism of certain cow's milk components. It is generally a benign condition with mild, nonspecific and highly individual symptoms limited to the gastrointestinal tract (diarrhoea, bloating and distension, flatulence and abdominal pain). The severity of symptoms varies with the amount of lactose; conditions under which lactose is consumed; and the ability to tolerate the lactose load.

Congenital lactase deficiency in infants is a rare condition. A primary lactase deficiency is the most common cause of cow's milk intolerance, affecting all age groups and may be life-long. Clinical manifestations usually only become evident at puberty or late adolescence. In contrast, a secondary lactase deficiency is a transient condition which develops secondary to bacterial or viral infection.

Diagnosis of lactase deficiency is made on the basis of a history of gastrointestinal symptoms, occurring after and aggravated by milk ingestion; response to an empiric trial of dietary lactose reduction or avoidance; a breath test demonstrating abnormal hydrogen levels; an abnormal lactose tolerance test; stool sample for reducing substances or acidic pH; and/or small intestinal biopsy to assess direct lactase enzyme activity.

Symptoms are alleviated by complete elimination or reduced consumption of lactose-containing foods. Most lactose intolerant adults, however, can consume some lactose without major symptoms, thereby reducing the need for strict elimination of dairy (excellent source of calcium, phosphorous, magnesium, vitamin A, riboflavin and protein). The literature is explored on how much is needed to cause actual clinical symptoms.

Controversial associations regarding the role of lactose intolerance in irritable bowel syndrome, infant colic and inflammatory bowel disease are discussed as well as the possible beneficial role in reducing the incidence of ‘developed society’ large bowel diseases in the black African population.

Public awareness and misunderstanding of lactose intolerance are at an all time high. Health professionals need to alleviate patients’ fears about lactose intolerance, discuss the importance of calcium-rich foods and recommend dietary strategies to improve lactose tolerance only when intolerance is clinically proven. With the help of a qualified dietitian, individual lactose tolerance threshold levels can be determined to adjust the amount of lactose that can be consumed comfortably at any one time. Strategies are discussed to ensure this inclusion of milk and other dairy products without implementing strict elimination diets.

CASE REPORT
This case report was embellished to illustrate various aspects of lactose intolerance.

A 20-year-old student presented to his general practitioner (GP) with a 3-day history of vomiting and severe diarrhoea. Based on a stool culture, a bacterial infection was diagnosed and the student was treated with the correct antibiotic. Eating yoghurt or drinking milk seemed to worsen his diarrhoea and the doctor advised milk avoidance until it had settled. The diarrhoea started improving 3-4 days later, and once his 7-day course of antibiotics was complete, his stools had normalised and his appetite returned.

On his return to campus, he had lunch (tuna mayonnaise sandwich, yoghurt and a cup of coffee with milk) at the cafeteria. That afternoon, he experienced abdominal cramping but attributed it to hunger pangs. To alleviate this, he ate a slab of chocolate and drank 250 ml flavoured milk. Approximately 1-2 hours later, the cramps worsened and he developed diarrhoea. He went back to the doctor, concerned that he had another ‘stomach bug’.

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Fig. 1. Dairy products that contain lactose.
Lactase deficiency was suspected. However, the student’s diet and lifestyle were evaluated. He had started...

Two weeks later, he revisited the GP, again with diarrhoea, severe cramping and bloating. The student followed instructions and the diarrhoea and cramps resolved. He managed to reintroduce dairy-containing foods, starting with lower lactose options, e.g. cheese and yoghurt, after a week. An intolerance of some kind.

• Food poisoning
• An allergic reaction to something which he had ingested
• An intolerance of some kind.

Screening

-skin testing
-enzymes
-antibodies
-jejunal biopsy

The following possible causes were considered:

- A possible second infection or incomplete treatment for the first infection
- Food poisoning
- An allergic reaction to something which he had ingested
- An intolerance of some kind.

The doctor and dietitian suggested he should determine his individual threshold for lactose tolerance so that he could still ingest calcium-rich dairy products without inducing clinical reactions.

The student was not convinced and enquired as to why he had previously been able to tolerate milk in his coffee, as well as chocolate and yoghurt on various occasions.

Being of black African descent, he had always had an underlying primary lactase intolerance with a particular threshold. The diarrhoea had resulted in damage to the villi and therefore affected lactase production, precipitating intolerance at a lower threshold level. Once the lactase had been adequately replenished, he could once again tolerate amounts of lactose lower than his normal threshold, but when he increased the intake of lactose by drinking milk frequently, symptoms developed again.

The doctor and dietitian suggested he should determine his individual threshold for lactose tolerance so that he could still ingest calcium-rich dairy products without inducing clinical reactions.

BACKGROUND INFORMATION

Adverse reactions to cow’s milk can be divided into the following:

• Immune reactions:
  - IgE-mediated
  - Non-IgE-mediated.
• Non-immune reactions – intolerance:
  - Enzyme deficiency (congenital, primary and secondary)
  - Malabsorption
  - Metabolic abnormalities
  - Psychological aversion.

DISTINGUISHING BETWEEN COW’S MILK ALLERGY AND LACTOSE INTOLERANCE

Although cow’s milk allergy and cow’s milk intolerance are different conditions, the terms are often used interchangeably, resulting in confusion in clinical practice. Cow’s milk allergy is an immunologically mediated reaction to cow’s milk proteins that may involve the gastrointestinal tract, skin, respiratory tract or multiple systems, i.e. systemic anaphylaxis. Cow’s milk intolerance refers to non-allergic, non-immunological reactions to cow’s milk such as disorders of digestion, absorption or metabolism of certain cow’s milk components. It is generally a benign condition with symptoms limited to the gastrointestinal tract. The most common cause of cow’s milk intolerance is lactase deficiency and it may be life-long. Table I summarises the difference between the two conditions.

LACTOSE INTOLERANCE

What is lactose and where is it found?

Lactose is the sugar found in milk and dairy products (Fig. 1). The lactose molecule is a disaccharide and it requires the digestive enzyme lactase to split it into the monosaccharides glucose and galactose in order for absorption to occur. Lactose content in dairy foods varies and may be influenced by the manufacturing process (heating, hydrolysis, fermentation) (see Table II).

Epidemiology and pathogenesis

Lactose intolerance literally means an inability to digest lactose because of a deficiency of the enzyme lactase,
located in the villus enterocytes of the small intestine.\textsuperscript{2-10} There are three main types of lactase deficiency:\textsuperscript{2,5,10}

- Congenital
- Primary
- Secondary

Lactase deficiency in infants (congenital) is uncommon because lactose is the principle sugar in human milk and the baby usually has enough lactase to digest the lactose sufficiently. Most adults lose some degree of lactase activity after puberty.\textsuperscript{2-10}

Primary intolerance is the most common carbohydrate intolerance and tends to affect all age groups. Typically, lactase activity declines with the initiation of complementary feeding and in early childhood to about 10% of the neonatal level. Clinical manifestations usually only become evident at puberty or late adolescence. Partially or undigested lactose remains in the gut and acts osmotically to draw water into the intestines. Colonic bacteria ferment the undigested lactose, generating short-chain fatty acids, carbon dioxide, hydrogen and methane gas.\textsuperscript{2-10}

Approximately 75% of the world’s population are affected by the primary lactase deficiency. Within various ethnic groups, it is present in up to 15% of people of northern European descent, 80% of blacks and Latinos and up to 100% of Asians and American Indians. The age of onset also varies between population groups but symptoms tend to appear during adolescence. Although 75-85% of white adults of northern European descent and some ethnic groups in India, Africa and Mongolia retain high levels of lactase, it remains half that of the other saccharides.\textsuperscript{2,5,6,8,11}

Maintenance of the lactase enzyme into adulthood is attributed to inheritance of an autosomal-dominant mutation that prevents the maturation decline of lactase expression. This genetic mutation is thought to be evolutionary, having developed 10 000 years ago when dairy farming was first introduced and spreading throughout the world with population migration. The highest incidence of lactose tolerance is in Sweden and Denmark (97%). Lactose favours calcium uptake and thus a lactose tolerance in these areas would have provided a selective advantage for greater health, reproduction and survival.\textsuperscript{2,6,8,12}

Secondary lactase deficiency is a transient condition which develops secondary to bacterial or viral infection causing destruction of the gut mucosal epithelial where lactase is normally active. It is most commonly caused by gastroenteritis and severe diarrhoea, AIDS or giardiasis, which typically damage the intestinal villi, thus reducing lactase activity. This condition may require dietary manipulation or gut rest in severe cases. Antibiotics and other drugs may also damage the epithelial cells. Regular lactase activity will resume once the cells have been able to repair.\textsuperscript{7}

Colonic flora are also important in the condition. Colonic adaptation occurs to some sugars that remain undigested from the small intestine (non-digestible oligosaccharides, lactulose). Lactulose ingestion decreases the colonic pH, thus increasing hydrogen excretion. This higher fermentative capacity may lead to a reduction in lactose intolerance symptoms.\textsuperscript{7,12}

**Clinical manifestations and symptoms**

The undigested lactose molecules and products of bacterial digestion result in predominantly gastrointestinal symptoms including diarrhoea, bloating and distension, flatulence and abdominal pain. The symptoms are generally mild, non-specific and highly individual. Persistent, severe gastrointestinal symptoms may indicate another disorder. Psychological and physiological factors may however also mimic the condition.\textsuperscript{2,4,5,8,11}

The severity of symptoms varies with the amount of lactose, conditions under which lactose is consumed, and the ability to tolerate the lactose load. Symptoms occur between 30 minutes and several hours after consuming lactose-containing food or drink. A person with low lactase levels won’t necessarily develop intolerance or symptoms after lactose intake.\textsuperscript{2,4,5,8,11}

**Diagnosis and laboratory tests**

Diagnosis of lactase deficiency is made on the basis of one or more of following:\textsuperscript{2,3,5,6,8,11,12}

- History of gastrointestinal symptoms, occurring after and aggravated by milk ingestion
- Response to an empirical trial of dietary lactose reduction or avoidance
- Breath test demonstrating abnormal hydrogen levels
- Abnormal lactose tolerance test
- Stool sample for reducing substances or acidic pH
- Small intestinal biopsy to assess direct lactase enzyme activity.

**Hydrogen breath test**

This is considered the gold standard for diagnosing lactose intolerance. It is simple, safe and non-invasive. The standard dose varies from the physiological dose of 12.5 g lactose (1 cup milk) to the tolerance test dose of 50 g lactose (1 litre milk) and should attempt to closely approximate the person’s usual lactose consumption. Intolerant individuals will demonstrate high fasting intestinal hydrogen production and 60 minutes after lactose ingestion, a secondary rise. An increase of >10-20 ppm above the baseline value is selected as the cut-off point. The test is however not lactose-specific as any undigested sugar in the intestine will be fermented by bacteria and produce hydrogen.\textsuperscript{2,3,6,14,15}

**Lactose tolerance test**

In lactose intolerance, an oral dose of less than 50g lactose will cause an increase in blood glucose less than 25 µg/100 ml above the fasting level, and gastrointestinal manifestations. Little or no increase in blood glucose indicates that lactose has not been broken down.\textsuperscript{7,8}

**Faecal reducing sugars**

This test is considered very reliable. After ingestion of a lactose-containing drink, a stool sample is collected and Fehling’s solution is added. The presence of lactose will cause a change in colour from blue to red. A simple kit is available to perform this test.\textsuperscript{6}

**Faecal pH test**

Collected stools after ingestion of a lactose-containing...
drink will be acidic (< pH 6) in cases of intolerance. This indicates fermentation of undigested sugars by the colonic bacteria. For absolute confirmation, a double-blind placebo-controlled food challenge should be done. This helps identify individuals who may be convinced of intolerance despite normal lactase levels and no symptoms after ingestion of reasonable lactose intakes.

Treatment and management

Symptoms are alleviated by complete elimination or reduced consumption of lactose-containing foods. Most lactose-intolerant adults can consume some lactose without major symptoms, thereby reducing the need for strict elimination of dairy products. Regular milk consumption in some lactose-intolerant individuals has been found to increase the threshold tolerance level at which diarrhoea occurs as a result of colonic adaptation. Tolerance also seems improved when lactose-foods are eaten as part of a meal. Some health professionals consider soy-based infant formulas to be the milk substitute of choice in lactose-intolerant infants. There are also lactose-free cow’s milk-based formulas available. Better tolerated dairy products include more solid and semi-solid forms such as cheeses (which cause delayed and slower gastric emptying) and yoghurt or cultured dairy products. Yoghurt and fermented milk products improve lactose digestion and eliminate symptoms of lactose intolerance. Yoghurt with lactic-acid-producing bacteria (including Lactobacillus and Streptococcus spp.) has showed health benefits for lactose intolerance in some studies. These beneficial effects are due to microbial beta-galactosidases present in the fermented milk products, delayed gastrointestinal transit, positive effects on intestinal functions and colonic microflora, reduced sensitivity to symptoms and enhancement of gastrointestinal innate and adaptive immune responses. Fermentation of dairy products also breaks down much of the lactose into its monosaccharides. Frozen yoghurt is however not well accepted as freezing destroys the microbial enzyme. Inconsistent results regarding the benefit of yoghurt may be due to differences in bacteria strains used, routes of administration, or investigational procedures; further robust studies will clarify these factors.

Lactose-containing medication, vitamin supplements and certain sweeteners/ additives may pose a problem for severely intolerant individuals. Commercial forms of the lactase enzyme exist in both liquid and tablet forms (Liquilacta, Lactaid) and various milk products have been treated with lactase (Parmalat Zymil) to facilitate better digestion and a less restrictive diet. There appears to be no need for these preparations however when the dosage of milk is limited to 1 cup.

Dairy products with added probiotics (Lactobacillus and Bifidobacterium spp.) may modulate gut microbial composition, leading to improved gut health and lactose intolerance symptoms. However, more research is needed regarding the therapeutic application of probiotics in this condition. When dairy products (and therefore excellent sources of calcium (75% of dietary calcium consumed), phosphorous, magnesium, vitamin A, riboflavin and protein) are eliminated, adequate nutrition must be provided in both growing children and adults to ensure appropriate bone growth, development and mineralisation, and to avoid rickets and osteoporosis. Dietary management strategies to increase calcium consumption in lactose-intolerant groups should include:

- Dairy foods consumed with meals
- Yoghurt and other fermented dairy products
- Calcium-fortified foods
- Using digestive aids
- Dairy foods daily in the diet to enhance colonic metabolism of lactose.

Good non-dairy sources of calcium, phosphorous, magnesium and protein include soya milk, soya yoghurt, tofu, canned fish (including the bones), seeds and nuts, beans, and other legumes, dark green leafy vegetables, oranges and some calcium-fortified breakfast cereals and fruit juices. Additional calcium supplementation is suggested to achieve the dietary reference intake for calcium (1 000-1 300 mg/day for adults). Individuals also need to obtain adequate vitamin D from moderate sunlight (approximately 30-60 minutes a day depending on age) and vitamin-D enriched foods, e.g. margarine.

Public awareness and misunderstanding of lactose intolerance are at an all time high. Scientific findings indicate that the prevalence of actual intolerance is grossly overestimated and many people erroneously believe they have developed intolerance symptoms and eliminate dairy products unnecessarily from their diet.

A recent study suggests an increase in individually, self-described ‘lactose intolerance’ with subsequent restriction of dairy and calcium intake that is a cause of serious concern. These individuals demonstrated reduced peak bone mass, increased incidence of osteopenia and greater risk of osteoporosis and bone fractures. Food challenges may be helpful in these cases, as seen in a study where individuals with self-reported lactose intolerance did not differ in response to milk chocolate samples containing different amounts of lactose. In two other reports, a third and a half of the lactose-intolerant subjects in the respective studies experienced symptoms to both a lactose-containing and lactose-hydrolysed milk under double-blind conditions, further highlighting the influence of social and cultural beliefs and attitudes towards milk tolerance.

Health professionals should alleviate patients’ fears about lactose intolerance, discuss the importance of calcium-rich foods, and recommend dietary strategies to improve lactose tolerance only when intolerance is clinically proven.

How much lactose can be tolerated?

Lactose intolerance is dose related; however, the degree of lactose malabsorption differs greatly among individuals, and a positive diagnosis can only be made if lactose-containing foods need to be eliminated. Most lactose-intolerant adults can consume some lactose without major symptoms, but the literature expresses differing views on how much is needed to cause actual clinical symptoms.

Age and the size (weight) of the individual will affect the actual amount of lactose that can be tolerated before symptoms develop; e.g., a 6-year-old child of 12 kg is unlikely to tolerate the same amount of milk that can be safely consumed by a 60 kg adult with the same degree of intolerance severity. Symptoms of lactose intolerance seem rarely to cause distress until more than 4-12 g lactose (100-240 ml milk) is ingested. Ingestion of low levels of lactose (below 7 g) shows no difference in non-specific intoler-
ance. A large psychological element was reported as no differences in symptoms were found between subjects who consumed 7 g of lactose and subjects who consumed no lactose. Consumption of quantities greater than 12 g (equivalent of 240 ml milk) usually leads to bloating, flatulence, abdominal cramps and diarrhoea. Another source suggests safe ingestion of 200-400 ml of milk daily. Adults with more moderate intolerance may be able to adapt, developing tolerance to more than 12 g lactose if amounts are increased gradually over 6-12 weeks.2,7,12,16

Symptoms tend to occur after large quantities of lactose (>50 g) are taken in a single dose. Cheese without lactose (hard and semi-hard cheese) or low in lactose (soft cheese contains only 10% lactose) can usually be consumed. Yoghurt with approximately one-third less lactose than milk is often well tolerated as previously mentioned.4,11,29,30

People with laboratory-confirmed low levels of lactase enzyme can safely consume 1 serving of milk (1 cup = 12 g lactose) with a meal or 2 servings of milk (2 cups) per day in divided doses with breakfast and dinner. Symptoms tend to occur as the lactose load is increased, with the majority of individuals having symptoms when the equivalent of 1 litre of milk is ingested in a single dose. People who describe themselves as severely ‘lactose intolerant’ may mistakenly attribute a variety of abdominal symptoms to lactose intolerance. In the majority of patients a lactose intake limited to approximately 1 cup of milk (240 ml) leads to negligible symptoms, and use of lactose digestive aids are unnecessary.2,21,31

To further demonstrate whether a usual lactose intake (2 cups milk daily with meals) could be consumed by lactose mal digesters, a double-blind, randomised crossover study was conducted in two groups with confirmed positive hydrogen breath tests – those who believed they were symptomatic and those who believed lactose intake did not induce symptoms. Both groups reported only minimal symptoms after intake of regular or lactose-free milk, reaffirming that most self-described lactose-intolerant subjects can easily tolerate 2 cups of milk daily when consumed in divided doses with breakfast and dinner.2,23

The high incidence figures for primary lactose malabsorption among groups grossly overestimate the number who will clinically react after drinking a glass of milk with a meal. Randomised, double-blind, controlled clinical trials have demonstrated that by using a few simple dietary strategies, those who malabsorb lactose can easily tolerate a dairy-containing diet that meets calcium intake recommendations. Health professionals can help these patients and the general public understand how to improve calcium nutrition by overcoming the enormous barrier of lactose intolerance and in so doing reduce the incidence of calcium-related chronic diseases in high-risk populations.6,20

**Lactose intolerance may offer protection against large-bowel diseases**

Research has found a reduced incidence of ‘developed society’ large-bowel diseases such as diverticulitis, colorectal adenomas and carcinomas, ulcerative colitis and Crohn’s disease in African black people. This disparity exists despite an adopted urbanised lifestyle and changes in dietary patterns including decreased fibre intake (from 30-35 g to 12-14 g daily). It is hypothesised that the increased concentration of substrate available for fermentation in the colon due to carbohydrate malabsorption in the group, compensates for the low dietary fibre intake. This would be protective of the large bowel, and helpful in the prevention of large-bowel disease in the African population.14

**Controversial areas**

Symptoms of irritable bowel syndrome (IBS) resemble the non-specific reactions of lactose intolerance. Subjects with IBS tend to self-diagnose lactose intolerance and eliminate dairy without evidence that the foods are solely responsible for symptoms. Research suggests that a lactose-restricted diet should be preserved only for patients who demonstrate symptoms of diarrhea, abdominal pain and flatulence during hydrogen breath testing, irrespective of what was previously reported. Certain individuals may benefit occasionally from a reduced lactose load; however, this should not be general practice in IBS patients. These patients should be reassured that small amounts of lactose are unlikely to cause abdominal symptoms even in lactose-intolerant individuals with demonstrated symptoms.18,25

Infantile colic has been linked to lactose intolerance; however, research remains inconclusive. Although there is no consensus as yet about its aetiology, it is likely to be multifactorial. Two randomised controlled trials found no benefit from lactase treatment of breast milk or cow’s milk formula. One double-blind placebo-controlled study found a modest but variable benefit from pre-incubation of foods with lactase. As yet, low lactose or lactose-free formulas or pretreatment of feeds with lactase are not recommended as treatment for colic.4

Inflammatory bowel disease (IBD; Crohn’s disease and ulcerative colitis) are commonly treated by exclusion of dairy products; however, most affected people are able to consume a glass of milk daily without discomfort. The prevalence of lactase intolerance tends to be greater in Crohn’s patients with small-bowel involvement than those with colon involvement or ulcerative colitis. In the latter colonic conditions, lactose malabsorption is as a result of ethnic risk, based on genetic factors. Bacterial overgrowth and/or small-bowel transit time may also be responsible for lactose malabsorption in Crohn’s disease.26

Despite these findings, dairy avoidance in these patients is extensive and can be attributed to patient misconceptions, as well as poor medical advice and minimal nutritional consultation. It is suggested that all IBD patients receive hydrogen breath tests to ensure better nutritional management, and avoid unnecessary dairy elimination and prescription of commercial lactase preparations.36

Conflicting evidence exists regarding links between lactose intolerance and an increased risk of cataract formation, development of diabetes and ovarian cancer.12

**TO SUMMARISE IN PRACTICE**

Each lactose-intolerant person, with the help of a qualified dietitian, should determine his or her own threshold and adjust the amount of lactose that can be consumed comfortably at any one time. Strategies to help with the inclusion of milk and other dairy products in the diet without experiencing symptoms include:14

- **Low amount of lactose consumed.** The larger the amount consumed, the greater the risk of symptoms. Most lactose-intolerant individuals can safely tolerate 1 cup of milk (12 g lactose), especially if taken with a meal or other foods, or 2 cups milk per day in divided doses at breakfast and dinner.

- **Consumption of a meal or solid food.** Consuming lactose with a meal or solid food may improve tolerance as it slows gastric emptying and delivery of lact-
to the colon, allowing more opportunity for any available endogenous lactase to digest the lactose.

- **Correct types of dairy food.** Certain dairy foods are better tolerated than others; e.g. full cream milk is better than lower fat milk. Chocolate milk may also be better tolerated than unflavoured milk, but the mechanisms by which cocoa reduces intolerance are unknown.

Other dairy products with lower lactose content than milk may be better tolerated, e.g. cheeses (Cheddar, Swiss, Parmesan, cottage cheese) and ice cream. Harder cheeses tend to have even less lactose, as the lactose-containing whey is removed from the curd during the cheese-making process. Lactose totally disappears in mature ripened cheeses. Fermented/cultured dairy products with beta galactosidase are better digested. Yoghurt, sour milk, and amas are among these. Yoghurt should contain live, active cultures as pasteurisation reduces the beneficial effects of the bacterial cultures on lactose digestion.

- **Lactose-reduced or lactose-free dairy foods or lactose digestive aids.** For the rare cases in which a patient is unable to tolerate even small amounts of lactose, or when large amounts of lactose-containing foods are eaten, commercially available lactose-reduced milk and other dairy products are available. A lactase preparation (liquid) can also be added at home to regular milk and left overnight. An oral enzyme replacement tablet, that can withstand the stomach's acidity, can be taken at the beginning of a meal. These products are expensive and are unnecessary if the equivalent of 1 cup milk/day can be tolerated.

- **Gradual increase of intake of dairy foods.** Tolerance to lactose can be improved by gradually increasing intake of lactose-containing foods. Lactose tolerance threshold can also be determined in this way. Elimination of lactose from the diet may actually worsen lactose intolerance in people with primary lactase deficiency.

REFERENCES