LACTOSE INTOLERANCE

Expert Reviewers

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Key Points:

- *Most lactose intolerance is due to primary lactase deficiency which is genetically determined*
- *Secondary lactase deficiency is transient and occurs mainly as a result of gastrointestinal illness*
- *Lactose intolerance can normally be diagnosed through dietary challenge*
- *Lactose intolerance is initially treated by minimising or avoiding lactose containing foods, however most people can tolerate one to two glasses of milk per day, in divided doses with food*
- *People with primary lactose deficiency should be encouraged to gradually and regularly increase their intake of milk until a level of tolerance is achieved*
- *Children who have developed secondary lactose intolerance as a result of infectious diarrhoea, may still safely receive milk*

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BACKGROUND

Lactose intolerance is the clinical syndrome that occurs, when the inability to digest lactose results in gastrointestinal symptoms. It is estimated that around 70% of the world's population are deficient in lactase.[1] However not all lactase deficiency results in lactose intolerance and it is likely that its prevalence is over estimated.

Most lactase deficiency is genetically determined. In general, people of Northern European descent have lower rates of lactase deficiency (2–30%) and people of Mediterranean, South American, African and Asian descent have higher rates (60–100%).[2,3] Both males and females are affected equally.[4] There have been two studies in New Zealand, reported in the 1980s, which suggest that people of Māori and Pacific origin have a higher prevalence of lactase deficiency than New Zealand Europeans.[5,6] A literature search did not reveal any recent follow-up studies to confirm these results.

Other physiological and psychological factors can contribute to gastrointestinal symptoms that mimic lactose intolerance.[7] Many people may believe they are lactose intolerant, but do not actually have impaired lactose digestion.[2]

- Lactose intolerance is NOT a milk allergy.
- A milk allergy is related to the protein in milk rather than the lactose.[2]
- Human breast milk contains 7% lactose and cow's milk 4.8%.[7]

THERE ARE FOUR TYPES OF LACTASE DEFICIENCY

Primary lactase deficiency is the most common reason for lactose intolerance (sometimes referred to as adult or late onset lactose intolerance). Lactase concentrations are at their greatest shortly after birth and rapidly decline after the usual age of weaning. The timing and rate of this decline is genetically determined. Primary lactase deficiency has a higher prevalence in those ethnic/geographical groups whose ancestors did not drink milk as a nutrient.[4,7] Onset of primary lactase deficiency is typically subtle and progressive over several years; however acute development is possible. The age of onset varies among ethnic populations, but it would be uncommon to be seen before two to three years of age (or before four or five years of age in European children).[1] Lactose intolerance may not become clinically evident until late adolescence.[8]

Secondary lactase deficiency (acquired) is transitory and can occur as the result of any gastrointestinal illness that alters the nature of the gut mucosa.[2] This is common in children with rotaviral (and other infectious) diarrhoea.[1] Giardiasis, cryptosporidiosis and other parasitic infections of the proximal small intestine often lead to lactose malabsorption.[1]

Secondary lactase deficiency may occur with coeliac disease, Crohn's disease and immune-related illnesses such as HIV.[1,4] In addition, drugs such as tetracycline and methotrexate can cause villous atrophy, resulting in secondary lactase deficiency. Alcohol is known to inhibit lactase and other enzymes, initiating or worsening lactose intolerance.[4]

Congenital lactase deficiency (alactasia) is the life-long absence of lactase.[2] This is an extremely rare condition that is apparent at birth, with the development of persistent diarrhoea soon after milk is introduced. Children with alactasia have otherwise normal intestinal mucosa.[9] This condition has been diagnosed in less than 50 people world-wide.[7]

Developmental lactase deficiency (neonatal) occurs in premature infants. This condition is usually temporary and rapidly improves as the intestinal mucosa matures.[9] Lactase and other disaccharidases are deficient until after 34 weeks gestation.[1]

GASTROINTESTINAL SYMPTOMS CHARACTERISE LACTOSE INTOLERANCE

In general, the symptoms of lactose intolerance are non-specific, highly individual and mild.[7] Symptoms usually occur between 30 minutes and two hours after ingestion of lactose.[2,7] Vomiting is rare[4] and severe gastrointestinal symptoms would be an indication to investigate other causes.[7]

Symptoms result from two main causes:[4]

1. Undigested lactose acts as an osmotic laxative (diarrhoea, abdominal pain)
2. Intestinal bacteria use lactose as a growth substrate (flatulence, dyspepsia, abdominal distension, stomach rumbling)

Symptoms are influenced by the degree of lactase deficiency and are dose dependent – the larger the amount of lactose consumed, the more frequent or severe the symptoms. The minimum dose of lactose to cause symptoms is variable but most people can ingest up to one or two cups of milk daily, without symptoms.[2]

Diarrhoea is more pronounced in children with secondary lactose deficiency than in those with primary lactose deficiency. Perianal excoriations due to acidic stools are common.[9]

Pathophysiology of lactase deficiency

Lactase is an enzyme that is located in the microvilli of the small intestine. Lactase splits and hydrolyses dietary lactose (a disaccharide sugar) into glucose and galactose (monosaccharide sugars) for transport across the cell membrane. In the absence, or deficiency, of lactase, unabsorbed lactose causes an influx of fluid into the bowel lumen, due to osmotic pressure. Unabsorbed lactose then enters the colon and is used as a substrate by intestinal bacteria, producing gas and short-chain fatty acids via fermentation. The fatty acids cannot be absorbed by the colonic mucosa, therefore more fluid is drawn into the bowel. A proportion of the lactose can be absorbed but the overall result of ingestion is a substantial rise of fluid and gas in the bowel, causing the symptoms of lactose intolerance.[2,7,9]

LACTOSE INTOLERANCE IS USUALLY DIAGNOSED BY DIETARY CHALLENGE

Step 1: Rule out other causes

Step 2: Dietary challenge

Step 3: Further investigation, if dietary challenge inconclusive

Accurate diagnosis of lactose intolerance can significantly relieve patient anxiety and avoid inappropriate investigation and treatment. Dietary challenge is the best way to achieve this in most situations. Laboratory testing will often not provide a definitive diagnosis and the availability of tests throughout New Zealand is variable.

Dietary Challenge

Lactose intolerance can be suspected in people who exhibit gastrointestinal symptoms following ingestion of milk or milk products. This can be confirmed by manipulation of diet. This diagnosis can be made by a GP and further investigation is rarely needed in clinical practice.[9]

The American Academy of Paediatrics recommends that when lactose intolerance is suspected, a lactose-free diet should be trialled for two weeks. However it is important that during this trial, all sources of lactose are eliminated – food labelling should be closely studied. If symptoms resolve over this two week period and then return with subsequent reintroduction of lactose containing foods, then lactose intolerance can be diagnosed.[1]

Self-diagnosis is not recommended as it could lead to unnecessary dietary restrictions and expense, lack of essential nutrients and most importantly, failure to detect a more serious gastrointestinal problem.[7]

If dietary challenge is inconclusive or self-reported symptoms are unreliable, then further investigation may be required.

Laboratory diagnosis of lactose intolerance

The role of laboratory tests in diagnosing lactose intolerance in New Zealand is limited. Although laboratory testing is often cited to aid in the diagnosis, many of these tests are not widely available and some lack sensitivity and/or specificity.

The breath hydrogen test is often referred to as the method of choice for laboratory diagnosis of lactose malabsorption but is not widely available throughout New Zealand. Breath hydrogen levels are measured after ingestion of 25–50 g of lactose (2 g/kg in children, maximum 50 g) after fasting overnight. Positive results are seen in up to 90% of patients with lactose malabsorption but false-negative results can occur and other factors such as gut motility disorders, small bowel bacterial overgrowth, a high fibre diet or smoking may increase breath hydrogen secretion unrelated to lactose digestion.[2,7,9] A specialist should be consulted to interpret the results of this test. The breath hydrogen test is technically difficult to perform in younger children and infants, for whom other tests may be more appropriate (faecal pH, reducing substances).

The lactose tolerance test is used infrequently, as it is less reliable than other diagnostic tests. Blood glucose levels are measured after ingestion of lactose – in lactase deficiency, glucose levels will not increase at a normal rate. False positives and false negatives occur in 20% of normal subjects due to the influence of variable gastric emptying and glucose metabolism.[2,9]

Faecal pH test is less commonly used as it is a non-specific marker for lactose (or other carbohydrate) malabsorption.[1] A pH of <5.0 suggests lactose intolerance.

Faecal reducing substances is a simple but non-specific test to detect the presence of lactose, glucose and fructose. A positive test suggests an absence of the corresponding enzyme. This is not offered in all areas of New Zealand because transportation delays (>3 hours from time of collection to testing) can cause false negative results.[10] A trace of positive reducing substances in a healthy breast fed infant is not uncommon and does not necessarily signify clinically significant lactose intolerance.

Small bowel disaccharidases is an invasive test involving duodenal biopsy and is very rarely used. It is not readily available throughout New Zealand. It is difficult to perform and results can be difficult to interpret. Results may be normal if lactase deficiency is confined to patches of the bowel.[8] This test may occasionally be considered in the context of secondary lactose intolerance where a gastroscopy is being performed to determine an underlying cause (e.g. coeliac disease, Crohn's disease, patient with protracted diarrhoea).

New diagnostic tests are also being developed, including a breath test using Carbon-13 labelled lactose.[9]

Differential diagnoses

When dietary challenge and laboratory tests prove inconclusive, alternative diagnoses should also be considered (see below).[2] Diagnostic tests are usually not needed for secondary lactase deficiency as it resolves upon treatment of the primary cause.

Differential diagnoses for lactose intolerance (adapted from Swagerty et al)[2]

Irritable bowel syndrome
Inadvertent laxative ingestion
Regional enteritis
Coeliac disease
Ulcerative colitis
Viral or bacterial infection
Cystic fibrosis
Parasitic disease e.g. giardiasis
Bowel neoplasm or polyp
Mechanical bowel compromise
Diverticulitis

LACTOSE INTOLERANCE CAN BE MANAGED IN MOST CASES BY DIETARY RESTRICTION

Step 1: Confirm diagnosis of lactose intolerance

Step 2: Determine how much lactose can be tolerated without symptoms

Step 3: Encourage gradual reintroduction of milk - this usually improves symptoms and tolerance

Initial treatment of lactose intolerance is to minimise or avoid lactose containing foods. However, it is important to retain an adequate calcium intake, including actual dairy products.[2]

Most people with primary lactose intolerance do not require a totally lactose free or severely restricted diet. One or two glasses of milk per day can usually be tolerated, if divided into small portions and taken with food (e.g. cereal).[11]

Yoghurt with live culture, curds and cheese (especially aged) is better tolerated because the lactose is partially hydrolysed by bacteria during preparation and gastric emptying is slower due to their thicker consistency.[9] Skim milk (green top) causes more severe symptoms than whole milk.[4]

Children may also tolerate up to one or two glasses of milk a day without symptoms.[1]

Chocolate milk and ice cream are better tolerated because their fat content delays gastric emptying.[2] Cow's milk substitutes are generally free of lactose and may be used (e.g. rice, soy) however their nutrient content is not equivalent to cow's milk and they should not be used in very young children. All mammalian milk, for example goats milk, contains varying amounts of lactose.[1]

Some people may choose to use lactase enzyme supplements, however these may not completely relieve symptoms and it is difficult to determine the effective dose. Enzyme supplements should be an adjunct, not a substitute for dietary restriction.[2] If milk is able to be tolerated in small amounts, enzyme supplements are unnecessary. Low-lactose milk is generally not necessary unless large quantities of milk are consumed, or in the rare case of non-tolerance to even small amounts of milk. In New Zealand, lactose-free, soy and goat's milk infant formulae are available on the pharmaceutical schedule, under special authority for children less than three years of age. Lactase enzyme supplements are not subsidised.

It is important to reassure patients that ingestion of lactose-containing products may cause symptoms, but these are transient and no harm is caused to the gastrointestinal tract.[1]

Increasing tolerance by exposure to lactose

People with primary lactose deficiency should be encouraged to gradually and regularly increase their intake of milk. Continual exposure often enhances the number and efficiency of colonic bacteria to metabolise lactose, thereby producing fewer symptoms. Total elimination of lactose from the diet may actually worsen the symptoms of intolerance when lactose is inadvertently ingested or reintroduced.[12]

Managing secondary lactose intolerance

Short periods of lactose intolerance are common in children after bouts of infectious diarrhoea. This can lead to unnecessary antibiotics and unwarranted avoidance of milk.[9] A meta-analysis of clinical trials found that most children with acute diarrhoea can safely continue to receive breast or undiluted animal milk.[13]

In children younger than three months, or in malnourished children, lactose intolerance after a bout of infectious diarrhoea may however be a significant factor that will influence recovery from the primary illness.[1] Lactose avoidance may be required for a short period.

LACTOSE INTOLERANCE IS NOT AN ALLERGY TO MILK

In cow's milk allergy, children are allergic to the protein in milk.

Cow's milk allergy is one of the most common food allergies in young children (prevalence between 2–6% of infants between 1 and 3 months of age).[1] The incidence in adults is much lower (0.1–0.5%).[14] Most children outgrow their milk allergy between 1 and 3 years of age.[1] However there is a strong trend in children who recover from a milk allergy, to develop an allergy to other food proteins (e.g. egg, soy, peanut) or an inhalant (e.g. pollen, dust mites, cat). Milk allergy is a strong risk factor for predicting children who will develop asthma, eczema or allergic rhinitis.[4, 14]

It is thought that exposure to cow's milk proteins commonly occurs prenatally. Breast fed infants are exposed to cow's milk and other food proteins ingested by the mother. In children who develop an allergy, the immune system becomes sensitised to the milk proteins and mounts an inflammatory response. It is thought that this is a hereditary condition, however the expression of this trait is dependent on both genetic and environmental factors.[14]

Despite possible in utero sensitisation, breast feeding is the best prevention for cow's milk allergy. There is no evidence to support the restriction of dairy intake during pregnancy or lactation to prevent cow's milk allergy.[14]

There are three types of clinical manifestation of cow's milk allergy;[4, 14]

Type 1 IgE mediated (Immediate): Develops within minutes to one hour of a small volume of cow's milk. Symptoms may be; eczema, urticaria, runny nose, cough, wheezing, vomiting, diarrhoea. Life threatening anaphylaxis is possible but rare.

Type 2 (Intermediate): Develops several hours after modest volume of cow's milk. Symptoms usually are vomiting and diarrhoea.

Type 3 (Delayed): Develops more than 20 hours after a large volume of cow's milk. Symptoms include diarrhoea with or without eczema.

Skin prick or specific IgE (RAST) tests can be used to diagnose a milk allergy in children with type 1 reactions. However nearly 60% of milk reactions in children are type 2 or 3 and are unlikely to give positive results. Diagnosis in this case is made by the 'elimination challenge test' (eliminating then reintroducing milk to the diet).

Differentiating between lactose intolerance and cow's milk allergy:

- Cow's milk allergy manifests during breast-feeding (due to cow's milk ingested by mother) or shortly after weaning. Lactose intolerance is usually seen after 2 years of age.
- Children with lactose intolerance can usually tolerate small amounts of dairy products, whereas in milk allergy, small traces usually cause symptoms.
- Differentiation is usually possible on the basis of clinical symptoms

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