

What factors need to be considered when prescribing for lactose intolerant adults?

Prepared by UK Medicines Information ([UKMi](https://www.ukmi.nhs.uk)) pharmacists for NHS healthcare professionals
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Date prepared: 16/08/19

Background

Lactose, a natural disaccharide sugar found in mammalian milk, is hydrolysed by the enzyme lactase in the small bowel to form glucose and galactose prior to absorption. Individuals with lactose intolerance have reduced or absent activity of the intestinal enzyme lactase resulting in malabsorption of lactose. When the undigested lactose reaches the colon it osmotically draws in fluid and is fermented by enteric bacteria. This may result in painful and persistent gastrointestinal (GI) symptoms e.g. abdominal bloating, flatulence, diarrhoea, nausea and abdominal cramps (1-4). The symptoms vary according to the quantity of lactose ingested, the patient's ability to digest lactose (3) and the amount and type of colonic flora (1).

Populations with Northern European ancestry have the lowest prevalence. By contrast, the prevalence of lactase deficiency is 50% to 80% in South Americans; around 60% to 80% in Africans and Ashkenazi Jews; and almost 100% in American Indians and some East Asians. Although not everyone with a lactase deficiency demonstrate the symptoms of lactose intolerance. (1, 5)

There are several types of lactose intolerance or lactase deficiency (hypolactasia) and the condition may be temporary or permanent in nature (2). The two most common types are:

1. Primary hypolactasia usually develops between the ages of 2 and 20 years. Affected individuals begin to produce less lactase after age 2 years but symptoms may not present until years later, if at all (2, 5).
2. Secondary (acquired) hypolactasia, which may result from injury to the small bowel secondary to viral or non-viral intestinal infection (1,2) or as a consequence of certain digestive diseases that impair lactase production e.g. inflammatory bowel disease, coeliac disease. Alternatively, a late onset version may develop with age because lactase levels naturally decline over a lifetime (2).

Answer

Lactose is widely used in pharmaceutical formulations as a diluent or filler in tablets or capsules. This includes prescription medicines, over-the-counter and complementary medicines. It is also used in lyophilized products, as a carrier in dry-powder inhalation products and in combination with sucrose to prepare sugar-coating solutions (6). Liquid preparations may also contain lactose (7).

The degree of lactose malabsorption varies widely among patients, but most individuals do not need a severely restricted or lactose-free diet (3). A meta-analysis (n=862) has compared symptoms in those with poor lactose digestion, following the intake of either lactose or placebo (8). Studies were included if the amount of lactose consumed was equivalent to that in a typical meal (7-25g). Where it was possible to compare the highest quality studies, the severity and incidence of GI symptoms were not statistically significantly different after lactose consumption compared to placebo. However, there were limitations to the meta-analysis.

In people with primary lactase deficiency the development of symptoms depends on how much lactose needs to be ingested before the available lactase is saturated. It has been suggested that 240ml of milk (12g of lactose) can be ingested by most people without developing symptoms (1). In a 2008 systematic review of 21 studies, most studies showed that a single test dose of 12g of lactose could be tolerated without other nutrients, whereas doses of 15-18g lactose could be tolerated when

given with other nutrients (9). However, some individuals may develop GI symptoms with lactose doses as low as 100mg to 200mg (7).

The lactose content of oral medications is generally small in comparison to the amount of lactose in many dietary substances, particularly dairy products (2). The dose of lactose in most pharmaceuticals is usually less than 2g per day. Therefore, unless an adult has severe lactose intolerance, it is unlikely that lactose in a conventional oral solid-dosage form will cause severe GI symptoms (6).

In a randomised, double-blind cross-over controlled trial, 77 patients with lactose malabsorption and symptoms of intolerance underwent two hydrogen breath tests following the ingestion of either a 400mg lactose capsule or a placebo capsule. Subjects also recorded the severity of any symptoms of intolerance using visual analogue scales (VAS). There was at least a 21 day washout period before crossover. No statistically significant difference in breath hydrogen excretion or severity of GI symptoms following ingestion of lactose was seen compared to placebo. On the basis of these findings, the authors suggest that lactase deficiency should not be considered a contraindication to the use of medicines containing 400mg lactose or less (10).

In one UK study, medications used for the treatment of GI disorders or symptoms were identified, and the lactose content and quantity of a sample of these was measured using high-performance liquid chromatography (HPLC). 31 lactose-containing and 40 lactose-free preparations were analysed. In those medications where lactose was present, lactose content ranged from 4mg (equivalent to 0.1ml milk) in a 40mg Losec® capsule to 600mg (equivalent to 12.7ml milk) in a 3mg Budenofalk® capsule. The authors calculated that, based on BNF doses, the amount of lactose that patients taking GI medications might ingest per day ranged from 4mg/day in Losec® 40mg to 10.2g/day with 150ml lactulose (equivalent to 0.1ml or 216ml milk respectively). The findings of this study showed that lactose is present in medicines used for a wide range of GI symptoms, which could result in symptoms of lactose intolerance in susceptible individuals. Lactose-free alternatives for all GI indications were identified. Liquid preparations of most medicines are lactose-free and may provide an alternative option in some cases. The authors emphasize that patients often take more than one medication and so cumulative exposure to lactose may occur. It is suggested that the lactose content of medicines should be considered in addition to dietary sources in the management of patients with lactose intolerance (11).

Healthcare professionals should be aware of the possible effects of lactose in medications. The presence of lactose in a medicinal product, together with medical assessment, should be considered as a possible underlying cause of apparent GI intolerance to medications (2,4).

There have been case reports of intolerance to lactose in medications (12-19), including following the inhalation of Intal® (cromolyn sodium) capsules via a turbo-inhaler (16). In the latter case, it is suggested that the symptoms occurred following oral or pharyngeal deposition and subsequent ingestion of lactose. In another case report describing lactose intolerance with tranilcypromine tablets, symptoms included diarrhoea and the author suggests that as a result, the patient did not absorb the active ingredient, resulting in loss of efficacy (12). Although published case reports are rare, lactose-containing medications may cause patient discomfort and subsequently affect patient concordance. Different routes of administration, brands or alternative medications may be necessary (2).

For patients with severe lactose intolerance, the lactose content of any medications should be determined prior to prescribing by consulting the relevant manufacturer of the product. The amount of lactose used may vary by manufacturer, product, formulation and strength (2). The Summaries of Product Characteristics (SPCs) for most branded and many generic UK medicines can be checked at: <http://www.medicines.org.uk/emc/>

Summary

- ◆ Lactose is widely used in pharmaceutical formulations as a diluent or carrier. This includes prescription medicines, over-the-counter and complementary medicines. In adults with lactose intolerance, ingestion of lactose may cause GI symptoms. The symptoms vary according to the quantity of lactose ingested, the patient's ability to digest lactose (3) and the amount and type of colonic flora (1).
- ◆ The dose of lactose in most pharmaceuticals is usually less than 2g per day. Therefore, unless an adult has severe lactose intolerance, it is unlikely that lactose in a conventional oral solid-dosage form will cause severe GI symptoms (6).
- ◆ On the basis of the findings of one randomised double-blind controlled study the authors suggest that lactase deficiency should not be considered a contraindication to the use of medicines containing 400mg lactose or less (10).
- ◆ One UK study has shown that lactose is present in medicines used for a wide range of GI symptoms, which could result in symptoms of lactose intolerance in susceptible individuals. As patients often take more than one medication, cumulative exposure to lactose may occur. The authors suggest that the lactose content of medicines should be considered in addition to dietary sources in the management of patients with lactose intolerance (11).
- ◆ Although published case reports are rare, lactose-containing medications may cause patient discomfort and subsequently affect patient concordance. Different routes of administration, a different brand of the same medicine or a completely different medicine may be necessary (2). Liquid preparations of most medicines are lactose-free and may provide an alternative option in some cases (11).
- ◆ For patients with severe lactose intolerance, the lactose content of any medications should be determined prior to prescribing by consulting the relevant manufacturer of the product. The amount of lactose used may vary by manufacturer, product, formulation and strength (2). The Summaries of Product Characteristics (SPCs) for most branded and many generic UK medicines can be checked at: <http://www.medicines.org.uk/emc/>

Limitations

The following issues have not been addressed in this Medicines Q&A:

- Patients with lactose allergy.
- Patients with galactosaemia.
- The diagnosis and treatment of lactase deficiency.
- Drug-induced lactose intolerance.
- Lactose intolerance in children and adolescents

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Date Prepared

16th August 2019

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Date of check

31st October 2019

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Search strategy

- Embase
 - [exp lactose intolerance/ or exp lactose tolerance/ or exp lactase deficiency/] and [exp lactose/ and exp drug formulation/]
 - [exp lactose/] and [exp excipient/] and [exp adverse drug reaction/]
 - [exp lactose/pr] and [exp adverse drug reaction/]
 - [exp drug formulation/] and [exp excipient/] and [exp lactose/pr] and [exp lactose intolerance/]
 - [exp excipient/] and [exp lactose intolerance/] and [exp lactose/pr]
- Medline
 - [exp lactose intolerance/] and [exp excipients/] and [exp lactose/]
 - [exp lactose intolerance/CI]
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