Lactose Intolerance: New Insights due to Blinded Testing?

Benjamin Misselwitz
Division of Gastroenterology and Hepatology, University Hospital Zurich, Zurich, Switzerland

All human newborns and basically all newborn mammals express the enzyme lactase in the small intestine. This enables the digestion of lactose and the ability to thrive on milk as the only nutrient. However, later in life lactase expression is downregulated in animals and most humans, a process which possibly facilitates weaning. After lactase downregulation, lactose will reach the colonic microbiota, resulting in the production of short-chain fatty acids, hydrogen and methane, which can potentially cause gastrointestinal symptoms.

5,000–10,000 years BC in central Europe, a mutation within the promoter of the lactase gene occurred, resulting in the persistence of lactase expression also in adults [1]. This LCT-13910C>T mutation has been of tremendous evolutionary advantage, increasing evolutionary fitness by up to 19% in each generation [2]. Lactase persistence enabled our farming ancestors to ingest milk in large quantities, providing a clean source of liquid, calories and vitamin D. Due to these benefits, the mutation in the lactase promoter spread and in central and northern Europe as well as in North America lactase persistence (resulting in lactose digestion) is now the most frequent phenotype. However, in most areas of the world, including most parts of Asia and Africa, lactase nonpersistence and lactose maldigestion (LM) remain the most frequent conditions. For European and North American physicians, it is thus important to realize that lactase nonpersistence and LM are not a disease but a normal human phenotype [3].

Lactose intolerance (LI) refers to the development of symptoms after ingestion of lactose. LI can explain symptoms for some patients with diarrhea and abdominal pain. Learning from experience, patients will decrease milk and calcium consumption, possibly resulting in an increased risk for osteoporosis and bone fractures [4].

LI is not synonymous with and should not be confused with LM. Symptom development depends on the amount of lactose ingested, the colonic microbiota, individual sensitivity and subjective expectations [5]. Patient history can therefore be misleading: when tested in a blinded setting, individuals with self-diagnosed severe LI were able to ingest up to 12 g of lactose (corresponding to 250 ml of milk) and some of these individuals did not even have the LM phenotype [6].

A 2010 NIH conference therefore proposed a new definition of LI [7]. LI now refers to the development of symptoms after blinded lactose challenge in an individual with LM. Strictly speaking, testing of LI would therefore be a two-step procedure. First, the LM phenotype should be established. For this task, many tools including genetic analysis, the H2-breath test and measurements of lactase expression in duodenal biopsies are available. For the assessment of LI, blinded testing would be required, but so far no validated clinical tools are available. Therefore, LI according to the NIH definition cannot be diagnosed in today’s clinical practice.

In the current issue of Digestion, Latorre et al. [8] report the first study where testing for LI has been performed according to the NIH definition. 121 healthy
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References


