Introduction

Chapter 1
INTRODUCTION

Lactose intolerance is a clinical condition in which humans are not able to digest milk sugar-lactose due to the lack of enzyme – Lactase−phlorizin hydrolase (commonly known as lactase). Lactase is disaccharides- composed of two mono saccharides- glucose and galactose. Lactase (β-galactosidase) enzyme is required for enzymatic hydrolysis of lactose (Fig.1) (Catanzaro R et al 2021; Lousie H et al 2018; Szilagyi A et al 2018; Misselwitz B et al 2019). Hippocrates first used the term lactose intolerance around 4000 BC (Lomer MCE et al 2007). When body is unable to synthesise enough lactase then lactose consumed through food is not digested leading to colonic fermentation. This causes gastrointestinal symptoms such as bloating, nausea, flatulence, diarrhoea, vomiting etc. intestinal injury can be one of the several causes leading to lactose intolerance (Matthews SB et al 2005; Misselwitz B et al 2019).

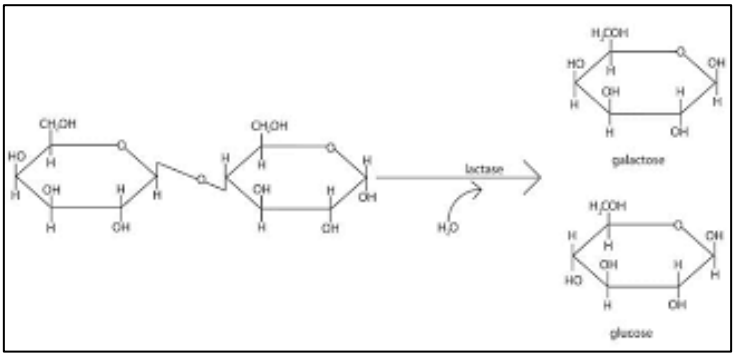

Figure 1 Chemical structure of lactose

Pathophysiology

In lactose tolerant individuals, the enzyme lactase phlorizin-hydrolase (lactase, a β-galactosidase) hydrolyses lactose into monosaccharides, glucose n galactose. These are then absorbed by intestinal enterocytes into the bloodstream, where glucose is utilized as a source of energy and galactose becomes a component of glycolipids and glycoproteins.

The enzyme has two active sites- one for hydrolyzing lactose, and the other for phlorizin and a range of dietary glycolipids. Lactase is present on the apical surface of enterocytes in the small intestinal brush border with its highest expression being in the mid-jejunum (Lomer MCE et al 2007). Initially this enzyme is produced as a 220 KDa precursor polypeptide which goes

through significant changes after post-transcriptional modification becomes matured protein 150 kDa. After hydrolysis of lactose, glucose is utilised as a source of energy whereas galactose becomes a component of glycolipid or glycoproteins.

In the absence or low production of lactase, lactose hydrolysis does not take place. This undigested lactose leads to fermentation in colon due to bacteria present in it. This results in massive production of short chain fatty acids, methane, carbon dioxide etc.

Prevalence of lactose intolerance

European countries such as Denmark and Ireland have prevalence rates as low as 4% lactose intolerance, whereas countries like the Czech Republic have 81% lactose intolerance. Asian countries have comparatively higher percent of prevalence than European countries. Asian countries such as Pakistan and India have 58% and 61% of lactose intolerance respectively whereas Yemen and South Korea have 100% of lactose intolerance. African countries such as Niger showed 13% lactose intolerance, whereas Malawi showed 100% lactose intolerance. Lactose intolerance was found to be 44% in Australia. North American countries showed 42%, whereas southern American countries showed 62.5% lactose intolerance (Christian LS et al 2017; Lomer MCE 2007; Solomons NW 2002; Kretchmer N 1971; Swallow DM 2003; Olds LC and Sibley E 2003). At times the decline in lactase synthesis occurs in childhood whereas in other it might happen during adolescence, ethnicity, physiological factors, diseases, injury are some of the factors determining it.

In Indian sub-continent it is observed to be 70% in southern India whereas 30% in northern India (Vrese DM 2001).

Lactose intolerance and its symptoms

Lactose intolerance occurs as lactase production decreases. Undigested lactose passes into the colon, part of the large intestine absorbs water from stool and changes it from a liquid to solid form, upon colonic fermentation leads to gastrointestinal symptoms such as bloating, acidity, diarrhoea, vomiting, borborygmi etc. Headache and nausea might also occur as a result of indigestion. Severity of symptoms occur with severity in maldigestion of lactose (Catanzaro R et al 2021; Szilagyi A et al 2018).

Lactose intolerance and genetics

Continuously production of lactase throughout life (lactase persistence, LP) is a genetically determined trait and is found at moderate to considerably high frequencies in Europeans and some African and Middle Eastern population. Lactase production decreases with increase in age.

Close association has been observed between lactase persistence and two polymorphisms, C/T13910 and G/A22018 upstream from the lactase gene1 8 9, CC/GG being associated with lactase non-persistence and lactose intolerance. It has been observed that decrease in lactase enzyme varies from one ethnic group to another. Chinese and Japanese lose 80%–90% within three to four years after weaning, whereas Asians and Jews can retain some 20%–30%, taking several years to reach the lowest level. It has been reported in studies that heterozygotes can still have severe lactose intolerance. Studies suggest that C ⁄ T13 910 is the dominant polymorphism with the C allele linked to a decline in lactase mRNA expression. Though, the precise mechanism of this fall in lactase after weaning is uncertain. (Anguita-Ruiz A 2020; Lomer MCE 2007).

Types of lactose intolerance

Lactose intolerance can be categorised into primary lactose intolerance, secondary lactose intolerance, developmental lactose intolerance and congenital lactose intolerance. Primary LI also known as lactase non-persistence is referred to as hereditary lactase deficiency, or adult-type hypolactasia. This type of lactose intolerant is genetic, irreversible, and usually develops during childhood. Secondary LI is caused due to any existing intestinal injury or surgery that might lead to low lactase synthesis and lactose malabsorption. This can occur at any age. Developmental lactose intolerance might occur in infants born prematurely- this usually last for a short period of time after a child is born. Congenital lactose intolerance is extremely rare, genetic (genes inherited from parents causes disorder). This condition is most common in Finland, where it affects an estimated 1 in 60,000 new borns (Szilagyi A et al 2018; Harvey L et al 2018; Matthews SB et al 2005).

Diagnosis of lactose intolerance

Lactose intolerance can be detected by various method. First most popular and old method is Lactose tolerance test- in this Lactose is orally consumed and then blood is analysed to observe rise in blood sugar. Secondly, we have Hydrogen breath test- in this lactose is orally consumed and a breath analyser is used to measure the hydrogen emitted. Third diagnostic test is Biopsy- lactase activity at jejunum brush border is studied. The fourth and expensive method is genetic test. Hydrogen breath test is mostly preferred as it is easy to administer, cost-effective and non-invasive (Robles L and Preifer R 2020).

Treatment

Various modes of treatments are available such as avoidance of milk, consumption of plant-based milk, introduction of yogurt and other probiotics and enzyme replacement therapy.

The most common advice that physicians give patients with LI is to avoid dairy foods (Savaiano DA et al 2013).

The hydrolytic capacity of probiotic strains can be used to reduce the actual amount of lactose in the product, as occurs in yogurt. It can also be used to increase the overall hydrolytic capacity in the small intestine. Saltzman JR in the year 1999 observed that 7-day supplementation with Lactobacillus acidophilus did not change hydrogen production or symptoms. Lactobacillus acidophilus is a bile-salt tolerant bacterium and improves lactose intolerance symptoms (de Vrese M et al 2015).

Rosada JL in the year 1984 showed in their study that 1 gm of b-galactosidase derived from k. lactis when added to 360 ml of cow's milk at the time of consumption eliminates significant incomplete sugar absorption in 60% -77% malabsorbers. Barrilas C in the year 1987 mentioned in their study that when 27 of 48 children who could not adequately digest whole milk, where subjected to whole milk along with lactase derived from k. lactis, then this enzyme was 82% effective.

Milk is a one of the most important sources of nutrients for children, adults and elderly and plays a significant role in maintaining the health of the individuals.

Several children (at varying stages-early childhood, childhood, adolescence) suffer from lactose intolerance leading to occurrence of symptoms such as severe abdominal pain, nausea and diarrhoea. These symptoms eventually interfere with the growth of children.

However little scientific evidence is available impact of lactose hydrolysed milk (LHM) and food products developed from LHM.

This study titled **"Assessing the presence of Lactose Intolerance among Children, Adults and Elderly of Urban Vadodara and Evaluating the Impact of Supplementing Lactose Hydrolysed Milk on their Quality of Life and Nutritional Status"** is been divided into four phases.

Phase I- Screening and identification of Lactose Intolerant (LI) subjects.

Phase II- Impact of supplementing Lactose hydrolysed milk (LHM) to lactose intolerant subjects.

Phase III- Organoleptic evaluation of food products developed from standard and lactose hydrolysed milk.

Phase IV- Development of IEC material.