Lactose Intolerance In Inflammatory Bowel Disease

Reviewed by:

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Introduction

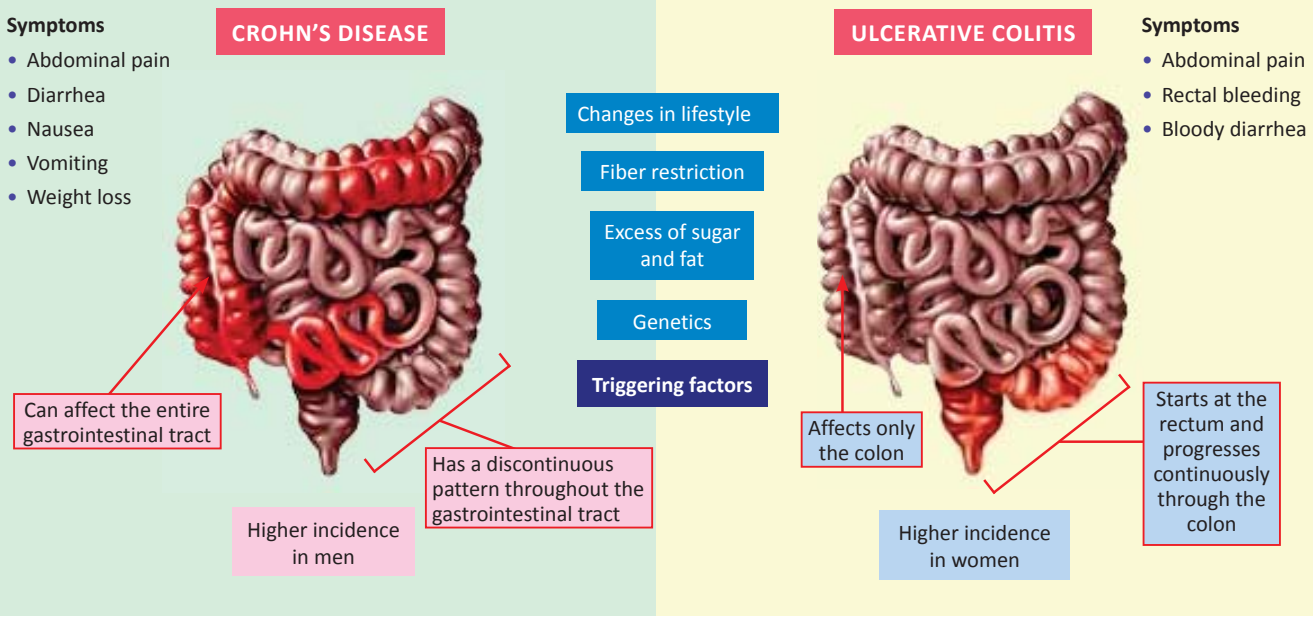
Inflammatory bowel disease (IBD) is defined as a chronic inflammation of the intestine that occurs due to host-microbial interactions in a genetically susceptible individual. It is an autoimmune disease characterized by inflammation of both the small and large intestine, wherein the body's own immune system attacks elements of the digestive system.[1] IBD, earlier considered to be a disease of the West, is increasingly being reported now from Asian countries. It is speculated that in few years India will have one of the highest disease burden of IBD across the globe.[2]

IBD primarily encompasses two conditions, namely, Crohn's disease (CD) and ulcerative colitis (UC). In Crohn's disease, there can be inflammation anywhere along the digestive tract lining; whereas in ulcerative colitis, there is long-lasting inflammation in some part (predominantly colon) of the digestive tract. A comparison of the main features of Crohn's disease and ulcerative colitis is depicted in Figure 1.[1,3]

Lactose intolerance in IBD

Although the cause of IBD is still unknown; it is believed to have a multifactorial etiology.[1] Diet has a major influence in pathogenesis of this disease and the association of dairy foods, lactose and IBD is still a topic of research. It has been found that about 2/3rd of the patients with IBD lose their ability to digest lactose (LNP; lactase non-persistence or LM; lactose maldigesters), and about 70% of the patients with IBD display lactose intolerance.[4,5] Lactose malabsorption causing intolerance is significantly greater in patients with Crohn's disease affecting the small bowel than in patients with Crohn's disease affecting the colon or ulcerative colitis.[5]

Figure 1: Main features of Crohn's disease and ulcerative colitis



Abbreviations: CD; Crohn's disease, UC; ulcerative colitis.

Adapted from: Barbalho SM, Bechara MD, Goulart RA, Quesada K, Gasparini RG, *et al.* Reflections about inflammatory bowel disease and vitamins A and D. *J Med Food.* 2016;19(12):1-6.

Lactose intolerance in IBD is of secondary type (Box 1).[6] The pathophysiological mechanism of lactose intolerance in IBD primarily involves deficient production of lactase enzyme by the small intestine due to chronic inflammation or damage of the intestinal lining (Figure 2).[7,8] Lactase deficiency results in the presence of unabsorbed lactose in intestine, which consequently leads to symptoms of lactose intolerance. Firstly, the increased osmotic load causes an increase in the intestinal water content. Secondly, lactose is fermented by the colonic microbiota resulting in production of short chain fatty acids and gases (hydrogen, carbon dioxide, and methane). The increased water content, short chain fatty acids and production of gases are responsible for symptoms of diarrhea, nausea and flatulence, respectively.[9]

Box 1: Types of lactose intolerance

Congenital

- No enzyme activity since birth

Primary

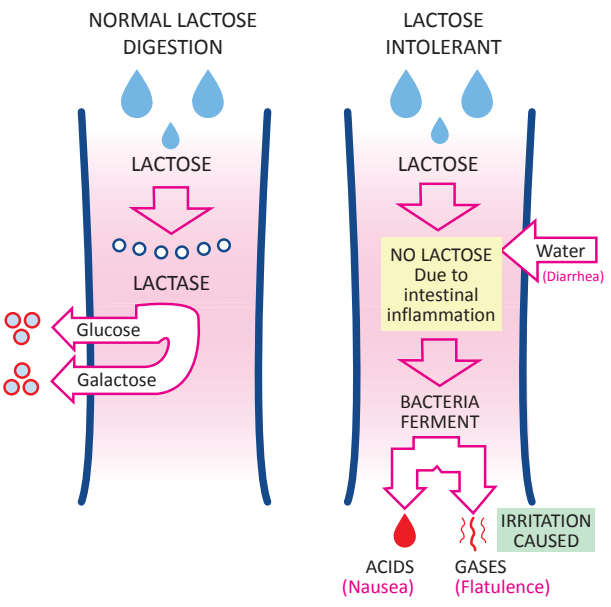
- Genetically predetermined reduction of enzyme activity during childhood or adolescence

Secondary

- Reduction of enzyme activity in response to diffuse intestinal insult—giardiasis, rotavirus, topical sprue, celiac disease, bacterial overgrowth, inflammatory bowel disease, intestinal resection

Adapted from: Rusynyk RA, Still CD. Lactose intolerance. *J Am Osteopath Assoc.* 2001;101(4):S10-S12.

Figure 2: Pathophysiology of lactose intolerance in IBD



Adapted from: Rana SV, Malik A. Breath test and irritable bowel syndrome. *World J Gastroenterol.* 2014;20(24):7587-7601.

Diagnosis and management of lactose intolerance in IBD: Focus on lactase enzyme supplementation

As discussed above, the symptoms of lactose intolerance might worsen the pre-existing condition of IBD in a patient. Such events can be disabling enough to cause an interference with routine activities. Hence, diagnosis and treatment of lactose intolerance in IBD patients is crucial. Diagnostic tests of lactose intolerance include lactose breath test, stool pH, small-bowel biopsy, genetic testing and lactose absorption test.[6,9] Amongst these, lactose breath test is the most widely used tool. The basis of this test is the activity of intestinal microflora fermenting ingested lactose leading to production of carbon dioxide (CO_2), hydrogen (H_2) and methane (CH_4).[10] Management of lactose intolerance primarily includes dietary modifications and lactase enzyme replacement.[11]

Dietary modifications

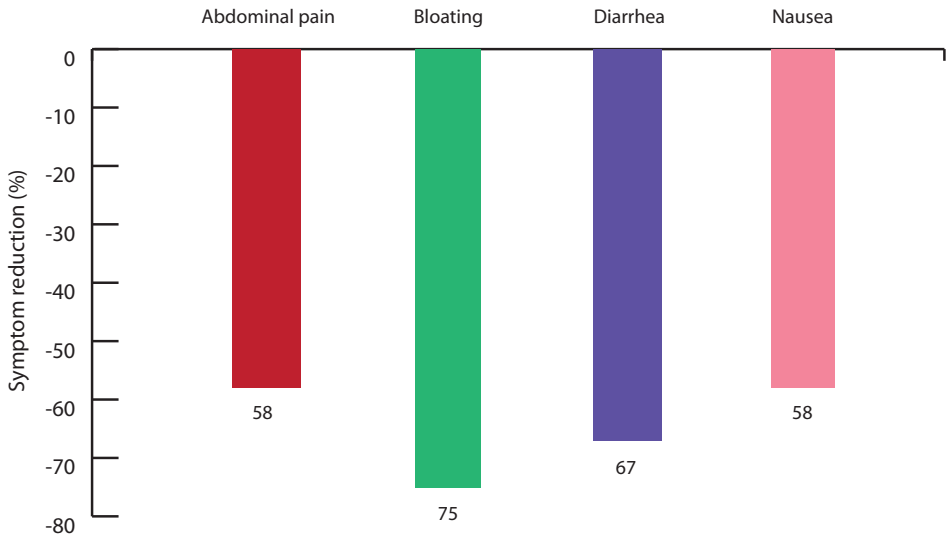
Symptom development following ingestion of lactose-containing foods and beverages is influenced by a number of factors like lactase activity, gastric emptying rates, fecal bacterial metabolites, colonic mucosal absorptive capacity, and intestinal transit time. Individual variation in the intensity of symptoms of lactose intolerance occurs due to differences in abdominal pain perception and psychological impact of pain and social discomfort.[12]

Most individuals with lactose intolerance follow a diet completely devoid of milk and dairy products, however, the National Institute of Health (NIH) guidelines suggest that ingestion of at least 12 grams of lactose in a single dose (equivalent to lactose content in 1 cup of milk) produces no or minor symptoms.[12] This is important since complete avoidance of dairy foods might result in significant nutritional risks such as lowered plasma and tissue content of calcium, potassium, vitamin D, vitamin B, and high-quality proteins. This low intake of minerals, vitamins, and dairy proteins can lead to weakened bones, fracture, osteoporosis, and other adverse health outcomes.[13] Also, individuals with IBD may remain symptomatic even on a dairy exclusion diet.[12] Thus, the main objective of dietary modification is to improve symptoms along with maintenance of an adequate intake of calcium, in order to prevent secondary bone disease caused by a milk-restricted diet.[14]

Lactase enzyme supplementation

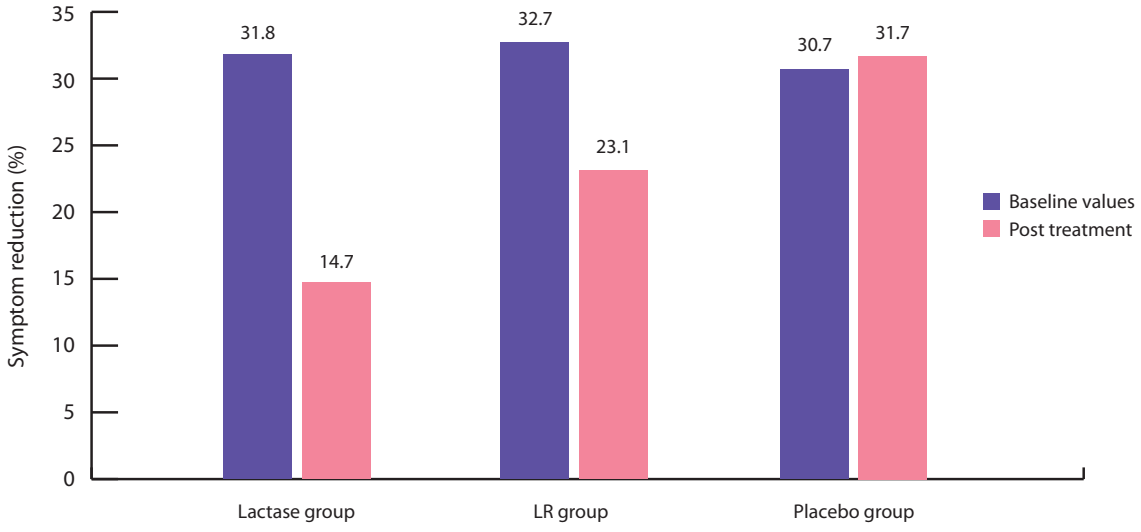
Oral supplementation of exogenous lactase enzyme is an important adjunct to dietary restriction approach. Numerous microorganisms, including bacteria, molds and yeast, are being used to produce lactase, including lactic acid bacteria, *Escherichia coli, Aspergillus niger, Kluyveromyces lactis* and *Kluyveromyces fragilis*. The exogenous lactase derived from these organisms is able to digest lactose into glucose and galactose, thus, ensuring improved absorption.[15,16] The lactase enzyme available in the tablet form is extracted from *Aspergillus* strain and can be taken immediately before and after consumption of milk products.[17]

Figure 3: Percentage reduction of symptoms of lactose intolerance upon oral administration of lactase enzyme



Adapted from: Fraissl L, Leitner R, Missbichler A. Novel formulation of neutral lactase improves digestion of dairy products in case of lactose intolerance. *Clin Transl Allergy.* 2011, 1(Suppl 1):P104.

Figure 4: Mean peak hydrogen concentration during lactose breath test



Adapted from: Ojetti V, Gigante G, Gabrielli M, et al. The effect of oral supplementation with Lactobacillus reuteri or tilactase in lactose intolerant patients: randomized trial. *Eur Rev Med Pharmacol Sci.* 2010;14(3):163-70.

Various studies have demonstrated that lactase enzyme provides a valid therapeutic strategy, with objective and subjective efficacy in patients with lactose intolerance.[9] An observational study by Fraissl *et al*,[18] showed a highly significant reduction of symptoms of lactose intolerance upon oral administration of lactase enzyme (Figure 3).[18] Another study[15] involving 60 patients, was conducted to assess the effect of supplementation with lactase enzyme when compared to *Lactobacillus reuteri* (LR) or placebo on hydrogen breath excretion and gastrointestinal symptoms in lactose intolerant patients during a standard

hydrogen lactose breath test. The study revealed a significant reduction of mean peak hydrogen excretion in lactase group and in LR group in comparison with the baseline values; with no change in the placebo group. Additionally, treatment effects with lactase supplementation were significantly superior to those with LR (Figure 4). Improvement in gastrointestinal symptoms was also highest in the lactase group.[15]

Conclusion

IBD is an autoimmune disease characterized by inflammation of both the small and large intestine. It has two variants – Crohn's disease and ulcerative colitis. Diet has a major influence in pathogenesis of this disease and the association of dairy foods, lactose and IBD is still a topic of research. Lactose intolerance in IBD is of secondary type and the symptoms of lactose intolerance might worsen the pre-existing condition of IBD in a patient, affecting his/her quality of life. Oral supplementation of exogenous lactase enzyme is an important adjunct to dietary restriction approach in these patients. Various studies have demonstrated that lactase enzyme provides a valid therapeutic strategy, with objective and subjective efficacy in patients with lactose intolerance.

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