Lactose Intolerance in Patients with Irritable Bowel Syndrome: Management Approaches

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An overview

Irritable bowel syndrome

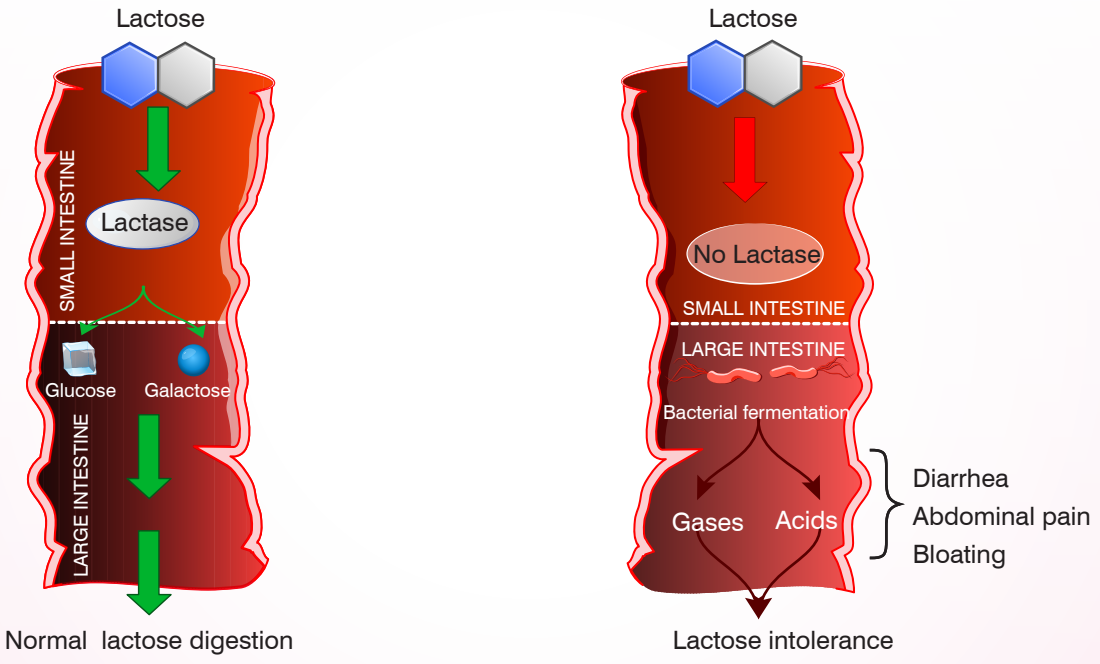
Irritable bowel syndrome (IBS) is a chronic and debilitating functional gastrointestinal disorder (FGID) characterized by altered bowel habits associated with abdominal discomfort or pain without apparent structural and biochemical abnormalities. Studies report that FGID have a prevalence of about 40% worldwide, with a higher occurrence in women than in men. In India, prevalence of IBS varies from 0.4% to 4.2%. Exact etiology behind IBS is still unknown. However, various factors contribute in its development. Altered gastrointestinal motility, visceral hypersensitivity, post infectious reactivity, brain-gut interactions, alteration in fecal micro flora, bacterial overgrowth, food sensitivity, carbohydrate malabsorption, and intestinal inflammation all have been implicated in the pathogenesis of IBS.[1-4]

According to the WHO DMS-IV code classification, IBS can be classified as either diarrhea-predominant (IBS-D), constipation-predominant (IBS-C), or with alternating stool pattern (IBS-A) or pain-predominant.[4] There is no specific test that can diagnose IBS. However, the diagnosis is based on specific symptoms known as the "Rome criteria." Rome IV is one of the accepted criteria for the diagnosis of IBS worldwide. However, in Indian population ROME-III criteria could be preferred over the ROME-IV criteria as it has higher sensitivity for IBS compared to the ROME-IV criteria for diagnosis of IBS.[3]

Lactose intolerance

Lactose intolerance is a clinical syndrome manifested by characteristic signs and symptoms when consuming products containing lactose and is caused due to deficiency of gastrointestinal enzyme lactase (Figure 1). Currently the prevalence of confirmed cases of lactose intolerance worldwide is about 57%. Typical symptoms of lactose intolerance are

Figure 1: Digestion and absorption of lactose in individuals with and without lactose intolerance[6]



abdominal pain, bloating, flatulence, diarrhea (in some cases constipation), borborygmi, nausea, and vomiting. On average, their onset occurs about one hour after ingestion of foods containing lactose, but they can also appear earlier or later. However, not all intolerant people develop symptoms of the same intensity. Growing evidence suggests that people with irritable bowel syndrome tend to develop more severe symptoms due to higher visceral sensitivity. All these symptoms have negative impact on the patient's quality of life. In fact, a high percentage of intolerant individuals experience anxiety, depression, and fatigue. These patients also develop severe eating disorders because patients tend to significantly reduce their food intake to avoid abdominal pain, diarrhea, and all other symptoms of lactose intolerance. The diagnosis of lactose intolerance is often made on a clinical basis and in response to an empirical study of dietary lactose avoidance. Nowadays, the breath test is considered the most practical and reliable method for diagnosing lactose malabsorption.[5,6]

Lactose intolerance in patients with IBS

The connection between IBS and lactose intolerance is not yet clearly understood. However, studies have shown that lactose intolerance is more common in patients with IBS and that IBS may be a contributing factor in patients with lactose intolerance.[6] It is estimated that lactose intolerance affects 4-74% of healthy people in different geographical areas and 4-78% of people with IBS. Lactose breath test also showed that 24-27% of IBS patients are affected by lactose maldigestion.[7]

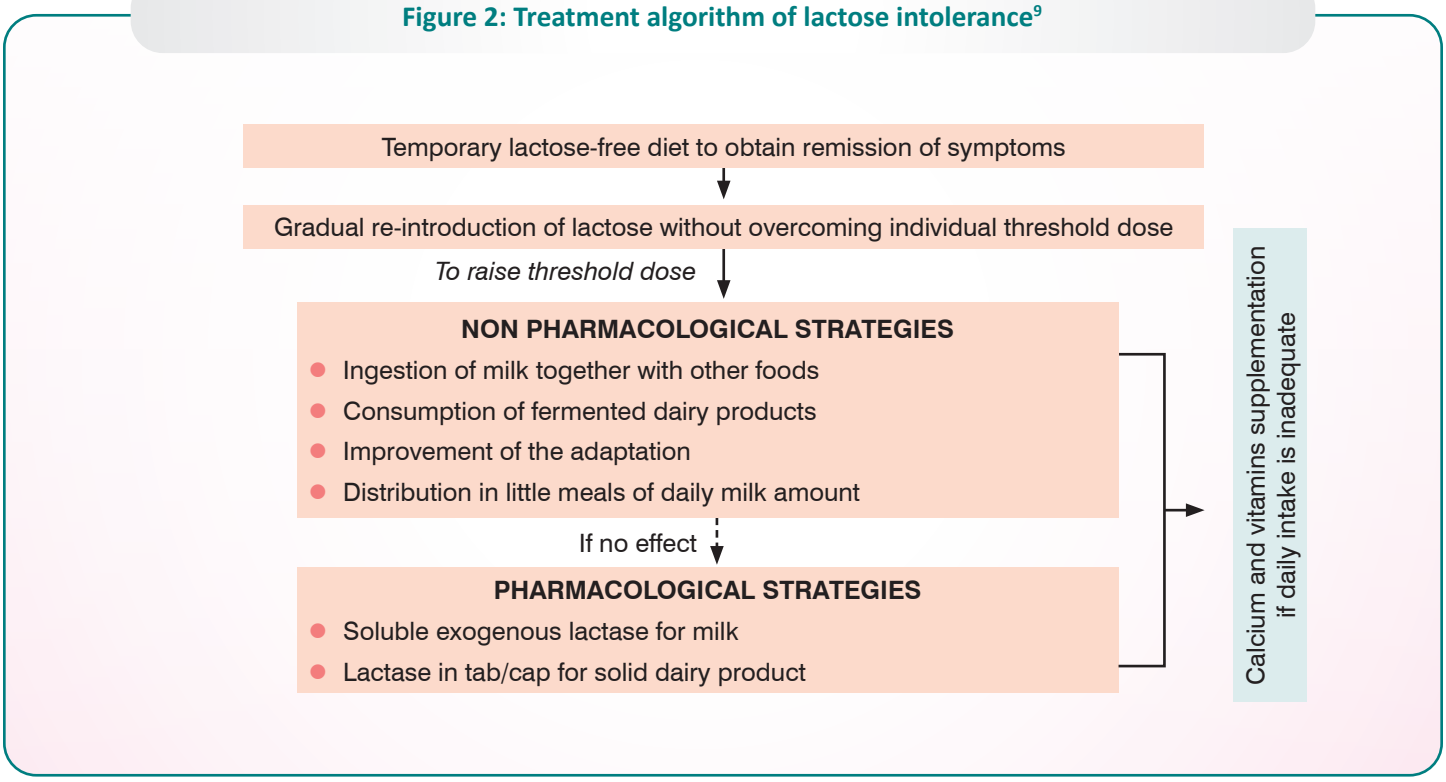
According to a study, 45% of IBS patients are affected by lactose intolerance. However, only thirty percent of those were able to link milk and other dairy products to their symptoms. This shows that some IBS patients reported symptoms of lactose intolerance despite not having lactose maldigestion. This suggests that lactose intolerance should be carefully evaluated in patients with IBS.[7]

An Indian study was also performed to evaluate frequency of lactose intolerance in patients with IBS and in its various subtypes as compared with healthy subjects. A total of 124 patients with IBS (Rome II criteria) and gender-matched healthy subjects were studied for lactose intolerance using the lactose hydrogen breath test (LHBT) and the lactose tolerance test (LTT). Results of the study showed that patients with IBS developed symptoms following lactose ingestion more frequently than healthy subjects (P = 0.01). The frequency of lactose intolerance in IBS-D was similar to that of other subtypes of IBS. This suggests higher frequency of lactose malabsorption and lactose intolerance in patients with IBS than healthy individuals.[8]

Management of lactose intolerance

As previously mentioned, patients with IBS tend to develop more severe symptoms of lactose intolerance due to higher visceral sensitivity. Therefore, treatment of lactose intolerance is aimed not only at reducing malabsorption, but also at improving gastrointestinal symptoms. Treatment is multimodal and includes both non-pharmacologic and pharmacologic options (Figure 2). In recent years, dietary modification has emerged as a promising key tool in the treatment of lactose intolerance in patients with IBS. In addition to dietary restrictions, treatment should also include maintaining adequate calcium intake to prevent secondary bone diseases caused by a low-dairy diet.[6,9,10]

Figure 2: Treatment algorithm of lactose intolerance[9]



> Patients with irritable bowel syndrome tend to develop more severe symptoms of lactose intolerance due to higher visceral sensitivity. Therefore, treatment of lactose intolerance is aimed not only at reducing malabsorption but also at improving gastrointestinal symptoms

Non-pharmacological approach

In patients with lactose intolerance, absolute restriction on the consumption of milk and milk-containing products is not recommended, as various studies suggest that patients with self-reported lactose intolerance can consume at least 12 g of lactose without symptoms. In addition, absolute restriction of dairy products can also have various nutritional and health consequences. Therefore, other effective treatment options should also be considered for patients with lactose intolerance. Nevertheless, milk intake in these individuals with lactose malabsorption should be carefully limited to less than 12 g of lactose per day, further divided into several small portions, and taken with other foods.[6,9]

In addition, colon adaptation by increasing lactose exposure is another attractive approach in the treatment of lactose intolerance. This is supported by the observation that introduction of lactose to the diet causes temporary and transient symptoms

Figure 3: Incidence of milk intolerance symptoms before and after administration of exogenous lactase in patients with lactose intolerance[14]

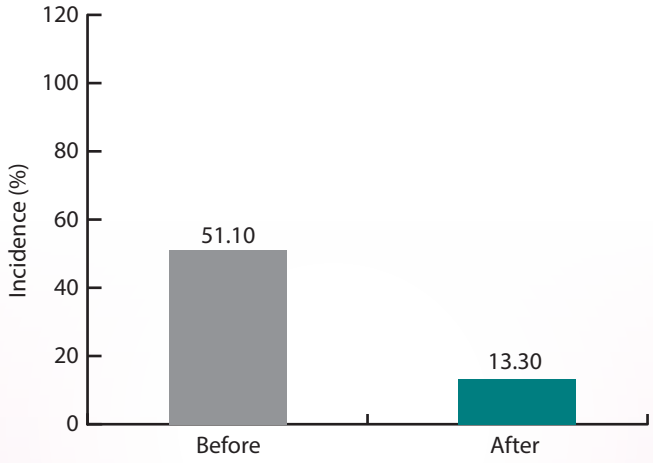
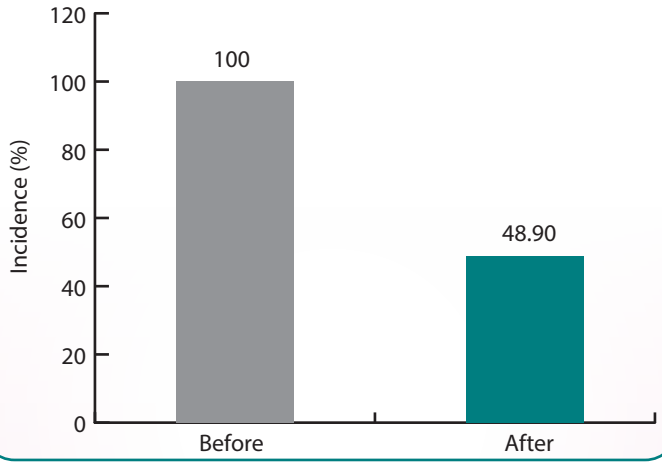


Figure 4: Incidence of lactose malabsorption before and after administration of exogenous lactase in patients with lactose intolerance [14]



in individuals. Since lactase from intestinal brush border is not an inducible enzyme, the reduction in symptoms can be explained by colonic adaptation.[11]

Pharmacological approach

Pharmacologic treatment strategies include enzyme replacement therapy with lactase from nonhuman sources to hydrolyze lactose. There are several commercially available lactase supplements that contain varying amounts of beta-galactosidase from different sources. Probiotics are live microorganisms that are non-pathogenic and have beta-galactosidase or lactase intracellularly and can help digest lactose absorbed by the host.[12]

Lactase enzyme supplementation therapy

Enzyme replacement treatment with microbial exogenous lactase represents a possible strategy for the treatment of lactose intolerance. This exogenous lactase is administered with the aim of hydrolyzing dietary lactose and has proven to be extremely effective in alleviating the symptoms of lactose intolerance.[13]

Evidence-based efficacy of lactase enzyme supplementation

Several studies conducted in different populations in the past have shown that lactose supplementation is an effective way to increase milk consumption and promote health in patients with lactose intolerance. He M. and his colleagues conducted a study[14] to evaluate the effects of exogenous lactase on lactose malabsorption and symptoms of lactose intolerance and found that administration of exogenous lactase could significantly reduce the occurrence of lactose malabsorption. Patients with a history of lactose intolerance were evaluated using a 25 g lactose tolerance test. Patients who met the inclusion criteria were challenged twice with 400 ml low-fat milk and 400 ml low-fat milk + 9000 Fcc lactase separately, in three days interval. The breath H_2 concentration and intolerance symptoms were tested in 4 hours after the challenge. The results showed that the administration of exogenous lactase resulted in a significant decrease in the

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incidence of milk intolerance symptoms (from 51.1% to 13.3%; Figure 3) and the incidence of lactose malabsorption (the abnormal expiration of H_2 decreased from 100% to 48.9% Figure 4). This shows that exogenous lactase supplementation can improve lactose absorption and symptoms of lactose intolerance.

In another study[15] conducted by Portincasa P. and colleagues, the effectiveness of single ingestion of a lactase preparation was tested. A total of 134 adults with hypolactasia (109 lactose intolerant; 25 lactose malabsorbers) were enrolled and underwent lactose H_2-breath testing plus either low (6750 U) or standard (11,250 U) doses of lactase. The results showed that after lactase ingestion, there was a time-dependent change of H_2 in breath; integrated H_2 levels decreased by 88% (standard dose) and 74% (low dose) in lactose intolerant patients (n=109). There was a significant decrease in symptom score with both doses of lactase; total symptom score decreased by 88% (standard dose) and 76% (low dose) in patients with lactose intolerance ($P < 0.0001$). These results support the conclusion that a single oral administration of lactase is very effective in reducing the symptoms and hydrogen excretion of hypolactasia, as assessed by a lactose-H_2 breath test. Therefore, lactase supplementation may be a better option than exclusion diets in patients with hypolactasia.

An Indian study[16] by Baijal R. and his colleague was also conducted to evaluate effect of lactase chewable tablets on clinical symptoms and hydrogen breath excretion in patients with lactose intolerance. A total of 47 patients with lactose intolerance were included. Results of the study showed a significant reduction in clinical symptoms and exhaled hydrogen excretion after oral supplementation with the enzyme lactase. The reduction in cumulative hydrogen breath levels over 180 minutes was 55% when patients received lactase compared to placebo. This shows that orally administered lactase enzyme significantly reduced clinical symptoms and hydrogen breath excretion in patients with lactose intolerance.

Conclusion

Lactose intolerance is a common health problem caused by a deficiency of the gastrointestinal enzyme lactase. Studies have shown that severe symptoms of lactose tolerance are more common in patients with IBS due to higher visceral sensitivity. In recent years, dietary modification has emerged as promising tool for treating lactose intolerance in patients with IBS. However, due to various nutritional and health consequences of dietary restriction, alternative effective treatment options should also be considered for patients with lactose intolerance. Oral supplementation with exogenously derived lactase enzyme appears to be a suitable approach to treat lactose intolerance in such a scenario as its effectiveness in relieving symptoms of lactose intolerance is well documented.

References

1. Varjú P, Gede N, Szakács Z, Hegyi P, Cazacu IM, Pécsi D, Fábián A, Szepes Z, Vincze Á, Tenk J, Balaskó M, Rumbus Z, Garami A, Csupor D, Czimmer J. Lactose intolerance but not lactose maldigestion is more frequent in patients with irritable bowel syndrome than in healthy controls: A meta-analysis. *Neurogastroenterol Motil.* 2019;31(5):e13527.
2. Sperber AD, Bangdiwala SI, Drossman DA, *et al.* Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study. *Gastroenterology.* 2021;160(1):99-114.e3.
3. Ghoshal UC, Sachdeva S, Pratap N, *et al.* Indian consensus statements on irritable bowel syndrome in adults: A guideline by the Indian Neurogastroenterology and Motility Association and jointly supported by the Indian Society of Gastroenterology. *Indian J Gastroenterol.* 2023 Apr;42(2):249-273.
4. Saha L. Irritable bowel syndrome: pathogenesis, diagnosis, treatment, and evidence-based medicine. *World J Gastroenterol.* 2014;20(22):6759-73.
5. Catanzaro R, Sciuto M, Marotta F. Lactose intolerance: An update on its pathogenesis, diagnosis, and treatment. *Nutr Res.* 2021;89:23-34.
6. Misselwitz B, Butter M, Verbeke K, Fox MR. Update on lactose malabsorption and intolerance: pathogenesis, diagnosis and clinical management. *Gut.* 2019;68(11):2080-2091.
7. Rana SV, Malik A. Breath tests and irritable bowel syndrome. *World J Gastroenterol.* 2014;20(24):7587-601
8. Gupta D, Ghoshal UC, Misra A, Misra A, Choudhuri G, Singh K. Lactose intolerance in patients with irritable bowel syndrome from northern India: a case-control study. *J Gastroenterol Hepatol.* 2007;22(12):2261-5.
9. Montalto M, Curigliano V, Santoro L, Vastola M, Cammarota G, Manna R, Gasbarrini A, Gasbarrini G. Management and treatment of lactose malabsorption. *World J Gastroenterol.* 2006;12(2):187-91.
10. Mattar R, de Campos Mazo DF, Carrilho FJ. Lactose intolerance: diagnosis, genetic, and clinical factors. *Clinical and Experimental Gastroenterology.* 2012;5:113-121.
11. Szilagyi A, Ishayek N. Lactose Intolerance, Dairy Avoidance, and Treatment Options. *Nutrients.* 2018;10(12):1994.
12. Usai-Satta P, Scarpa M, Oppia F, Cabras F. Lactose malabsorption and intolerance: What should be the best clinical management? World Journal of Gastrointestinal Pharmacology and Therapeutics. 2012;3(3):29-33.
13. Ibba I, Gilli A, Boi MF, *et al.* Effects of exogenous lactase administration on hydrogen breath excretion and intestinal symptoms in patients presenting lactose malabsorption and intolerance. *BioMed Research International.* 2014 (2014); Article ID 680196:7
14. He M, Yang Y, Bian L, *et al.* Effect of exogenous lactase on the absorption of lactose and its intolerance symptoms. *Wei Sheng Yan Jiu.* 1999; 28(5):309 11.
15. Portincasa P, Di Ciaula A, Vacca M, *et al.* Beneficial effects of oral tilactase on patients with hypolactasia. *Eur J Clin Invest.* 2008;38(11):835-44.
16. Baijal R, Tandon RK. Effect of lactase on symptoms and hydrogen breath levels in lactose intolerance: A crossover placebo-controlled study. *JGH Open.* 2020;5(1):143-148