The Connection Between Celiac Disease & Lactose Intolerance

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Celiac disease and lactose intolerance: An overview

Celiac disease (CD), also known as "celiac sprue", is a chronic inflammatory disorder of the small intestine resulting from both environmental (gluten) and genetic factors (human leukocyte antigen (HLA) and non-HLA genes).[1,2] This autoimmune disorder originates by an aberrant adaptive immune response produced by ingestion of dietary gluten products in the genetically susceptible individuals worldwide.[1] The prevalence rate of CD ranges from about 0.5-1% being more prevalent in patients with diabetes, autoimmune disorders or relatives of patients with CD as they are at a higher risk of shared HLA typing.[2] The clinical presentation of CD varies with age and is manifested by gastrointestinal, extraintestinal or no signs of symptoms at all as listed in table 1.[3]

Table 1: Clinical features of celiac disease

Symptoms	Extraintestinal manifestations
Gastrointestinal • Diarrhea • Abdominal pain • Bloating • Constipation	Arthritis Aphthous stomatitis Dermatitis Herpetiformis Osteoporosis/Osteopenia Elevations in transaminases Infertility
Nutritional deficiency • Anemia –iron deficiency → Folate deficiency • Vitamin D deficiency → Rickets → Hypocalcemia • Vitamin K deficiency → Coagulopathy	Recurrent abortions Neurologic • Ataxia • Epilepsy Psychiatric • Anxiety • Depression
Growth • Short stature • Delayed puberty	

Adapted from: Barker JM, Liu E. Celiac Disease: Pathophysiology, Clinical Manifestations and Associated Autoimmune Conditions. *Adv Pediatr.* 2008;55:349-365.

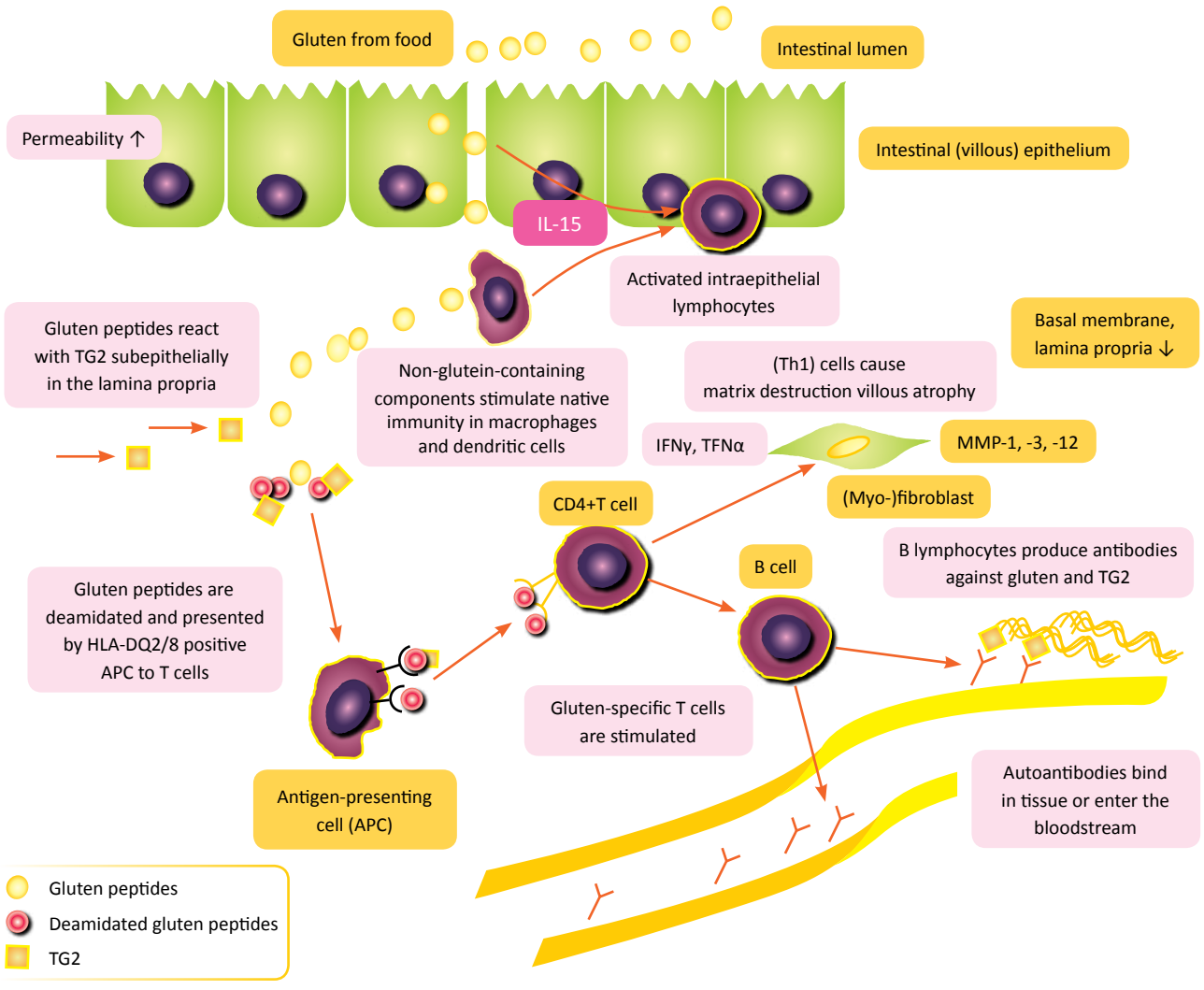
The pathophysiology of CD is unique from other autoimmune diseases and occurs due to genetic predisposition (either HLA-DQ2 or HLA-DQ8), presence of well defined precipitating factor (gluten), and existence of highly sensitive and specific auto-antibodies against the naturally occurring human enzyme, tissue transglutaminase (TG2).[3,4] The process initiates due to the presence of gluten, an alcohol-soluble fraction of wheat protein, which is consumed in large quantities (10–20 g per day) as part of the normal food intake. However, some of these gluten peptides do not get degraded by the gastrointestinal enzymes but are instead taken up across the epithelium of the small-bowel mucosa. In the small bowel mucosa these gluten peptides are presented on the antigen-presenting cells of people with the HLA types HLA-DQ2 or HLA-DQ8 (about 90% and 10% of persons with celiac disease, respectively) thereby causing stimulation of gluten-specific T cells (Figure 1).[4] Hence, the diagnosis of CD is suggested by the presence of TG auto-antibodies but is established by biopsy of the small intestine by upper intestinal endoscopy.[3]

Lactose intolerance (LI), on the other hand is a common gastrointestinal condition encountered due to the inability of the affected individual in digesting and absorbing dietary lactose. It presents with mild to moderate gastrointestinal symptoms, including abdominal pain, flatulence and diarrhea.[5] A slew of studies have demonstrated the prevalence of LI in patients with CD. This is usually encountered due to the presence of dietary proteins, such as those present in cow's milk. These proteins have known to induce CD-like symptoms in the affected individuals.[6] Hence, the diagnosis of LI in a patient with CD and vice versa is extremely important for the proper management and treatment of both the conditions.[7]

The connection between celiac disease and Lactose Intolerance

Celiac disease and LI are relatively common diseases, with symptoms occurring after ingestion of certain food components. In CD, ingested gluten (a protein storied in wheat, rye or barley) induces intestinal inflammatory disease in the susceptible individuals causing an array of gastrointestinal and extra intestinal symptoms. Hence, the patients with CD lead a strict gluten free diet throughout their life.[7] However, in spite of a total gluten-free diet many patients do not have a total histological or clinical recovery.[8] This is encountered due to two main reasons. Firstly,

Figure 1: Pathophysiology of celiac disease



Abbreviations: TG2; Transglutaminase 2, IL-15; Interleukin-15, Th1; T helper cells 1, IFN-γ; interferon gamma, MMP; Matrix metalloproteinase.
Adapted from: Schuppan D, Zimmer K-P. The Diagnosis and Treatment of Celiac Disease. *Dtsch Ärztebl Int.* 2013;110(49):835-846.

due to the presence of trace amounts of gluten in the diet and secondly, due to probable intolerance to a non-gluten food item. In context to the latter point, secondary LI has found to be as one of the commonest non-gluten food intolerances encountered in the patients with CD.

In newly diagnosed CD patients, secondary LI is common due to the loss of lactase, an enzyme that digests milk sugar along the lining of the small intestine.[9] The lining of the small intestine usually contains hair-like projections called villi which are lined by enterocytes, These villi further have hair-like projections called microvilli which are also called as the brush border. Enzymes responsible for digesting sugars (as well as breaking down products of protein) are found in the brush border and are called brush border enzymes. One of these brush border enzymes is lactase which helps in the digestion of sugar lactose found in milk. However, in patients with CD as the mucosa (or lining) of the small intestine is damaged, the villi become shortened or even completely flattened. This results in a decrease in the number of brush border enzymes like lactase leading to LI in patients with CD.[10]

Although a high prevalence of LI is seen in patients with CD the vice versa is also true. In context to this, a retrospective study was conducted by Ojetti et al[6] to evaluate the prevalence of CD in patients with a positive H2-lactose breath test compared to a control group. In this study, 54 patients (15 males/39 females; mean age 37.8 +/- 7 years) with a positive H2-lactose breath test and a negative H2-glucose breath test were matched on the basis of their sex and age to 50 blood donors drawn from a similar population who served as controls. The results of this study demonstrated that a high prevalence of CD was observed in patients with a positive H2-lactose breath test as compared to the healthy controls. Apart from secondary LI, an association between CD and primary lactase deficiency (PLD) also exists. In context to this, a study was conducted by Basso et al[11] on

188 controls and 92 biopsy-proven CD patients to evaluate the association of PLD and CD in both the groups. The results of this study demonstrated that, hereditary lactase deficiency was frequent in patients of the CD group as compared to the control population.

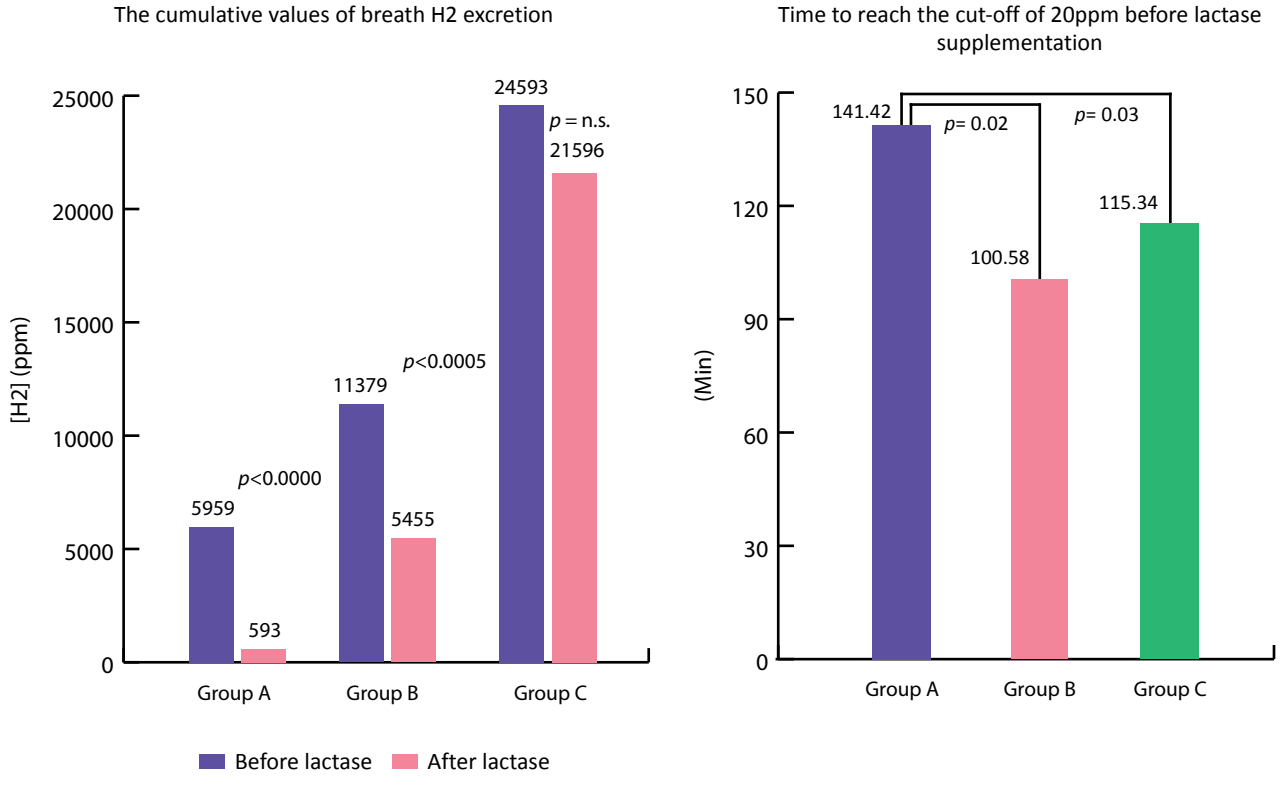
Hence, as both CD and LI are relatively frequent diseases the diagnosis of the connection between both these conditions is highly warranted for prompt and apt treatment of both the diseases.

Management of lactose intolerance in celiac disease: Focus on lactase enzyme supplementation

The management of CD is clear and well established and is achieved by lifelong avoidance of gluten, found in wheat, rye and barley.[3] However, in addition to this, as patients with CD may have accompanying brush border lactase deficiency secondary to damage to surface epithelial cells hence, milk and dairy products should also be completely avoided in the first period of treatment.[1] In such patients the lactose intolerance symptoms can continue for as long as 6 months to 2 years after initiation of 100% gluten-free diet.[10] Hence, apart from following a gluten free diet, supplementation of digestive enzymes like lactase provides a reliable, intriguing and convenient adjuvant treatment of LI in patients with CD.[12]

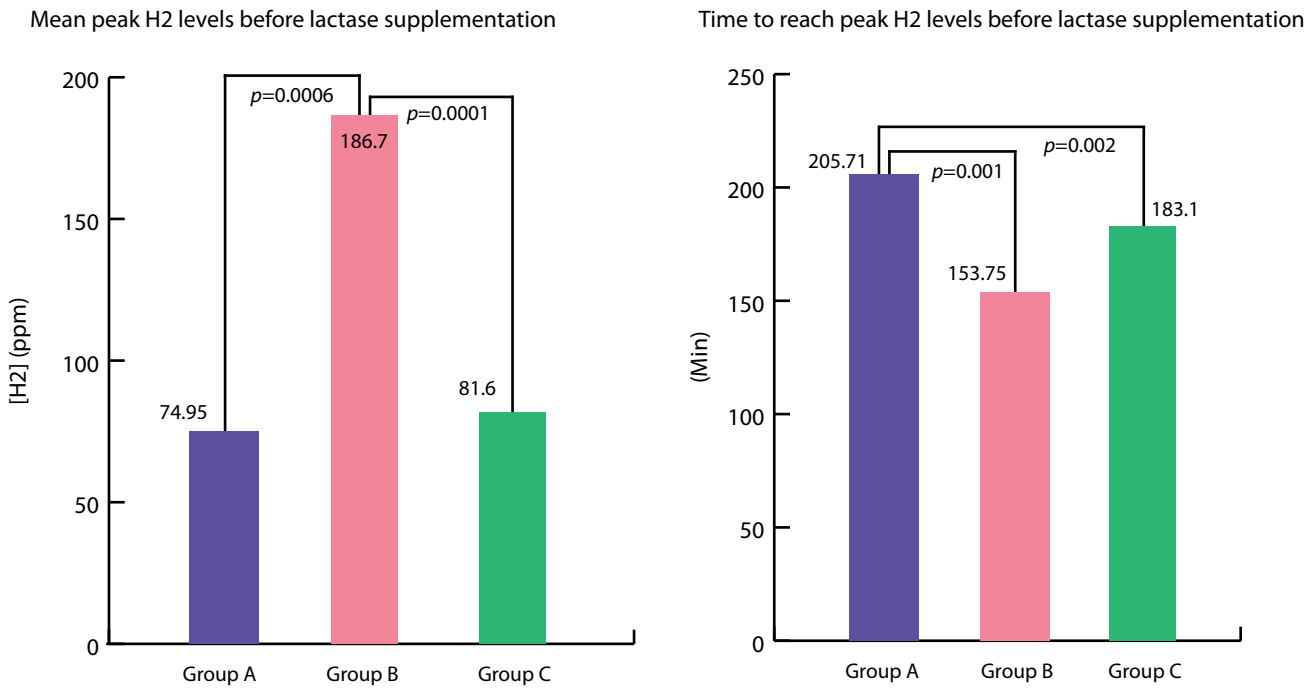
Lactase, an enzyme produced by intestinal villi, hydrolyzes lactose into galactose and glucose. In conditions of LI in CD, replacement of native lactase through the use of exogenous enzymes, derived from yeast or fungi, with microbial exogenous lactase (obtained from yeasts or fungi) may be considered a reliable therapeutic option. Exogenous lactase is usually administered with milk, or as capsules/tablets before consuming dairy products.[12] A slew of studies have established the efficacy of lactase supplementation in LI in patients with CD. In context to this, a study was conducted by DiPalma *et al*[13] on 10 healthy symptomatic lactose malabsorbers to evaluate the effect of lactase on symptom and breath hydrogen response. The results of this study demonstrated that a dose-related decrease for bloating and flatus was evident in the lactose malabsorbers when lactase was given before the ingestion of lactose. On the similar grounds another study was conducted by Ibba *et al*[14] to evaluate the efficacy of lactase supplementation on hydrogen breath excretion in patients with lactose malabsorption. A total of 96 consecutive patients with positive H2 Lactose Breath Test were enrolled for the study and their mean peak H2 levels, the time to reach the peak H2, the time to reach the cut-off value of 20 ppm, the cumulative breath H2 excretion, the areas under the curve, and a Visual Analogical 10-point Scale for symptoms were calculated. The results of the study demonstrated that,

Figure 2: The cumulative values of breath H2 excretion and time to reach the cut-off of 20 ppm before lactase supplementation



Adapted from: Ibba I, Gilli A, Boi MF, Usai P. Effects of exogenous lactase administration on hydrogen breath excretion and intestinal symptoms in patients presenting lactose malabsorption and intolerance. *Biomed Res Int.* 2014;2014:680196.

Figure 3: The mean peak H2 levels and the time to reach peak H2 levels before lactase supplementation



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following the administration of lactase, H2 Lactose Breath Test became negative in 21.88% of the cases (group A), while mean peak H2 levels were 74.95 ppm versus 7.85 (p<.0000). The H2 Lactose Breath Test were still positive in 17.71% of the cases (Group B), with the H2 level 20 ppm above the baseline, but the peak H2 levels significantly lower than those observed at the baseline test (186.7 ppm versus 66.64) (p<.0000). In addition to this, the H2 Lactose Breath Test were still positive in 60.41% of the cases (Group C) with the peak H2 levels similar to those observed at the baseline test (94.43 versus 81.60 ppm) (Figure 2 and 3). Hence, the results of this study demonstrated that a significant variability was evident in the symptoms of the patients with lactose malabsorption who were administered with lactase.

Hence, administration of lactase constitutes to be an intriguing therapeutic option and a tailored holistic approach for the management of LI in CD patients.

Conclusion

Celiac disease (CD) is a chronic inflammatory disorder of the small intestine resulting from both environmental (gluten) and genetic factors. Lactose intolerance (LI) is commonly encountered in patients with CD due to the loss of the lactase enzyme along the lining of the small intestine. Hence, management of LI in CD is achieved by lifelong avoidance of gluten along with supplementation of digestive enzymes like lactase. This holistic supplementation of lactase serves to be a reliable, intriguing convenient and tailored adjunctive treatment approach for effectively managing LI in patients with CD.

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