Nutritional Consideration in Celiac Disease and Nonceliac Gluten Sensitivity

Rishi D. Naik, MD, Douglas L. Seidner, MD,
Dawn W. Adams, MD, MS*

KEYWORDS

• Celiac • Nonceliac gluten sensitivity • Gluten • Nutritional deficiencies
• Gluten-free diet • Drug development

KEY POINTS

- Celiac disease is a chronic enteropathy of the small intestine, which leads to various gastrointestinal and extraintestinal symptoms and is associated with specific micronutrient deficiencies.
- A strict gluten-free diet is currently the only therapy for nonrefractory celiac disease and typically leads to healing of the small intestine and improved absorption of nutrients.
- Nonceliac gluten sensitivity typically does not damage the small intestine and, therefore, is marked by symptoms that improve with gluten cessation, rather than significant nutritional deficiencies.
- A gluten-free diet needs to be monitored because it can lead to nutritional deficiencies.
- Adherence to a strict gluten-free diet in patients without celiac disease nor non-celiac gluten sensitivity is not advised.

INTRODUCTION

Celiac disease (CeD) is an autoimmune disorder in which gluten and gluten-related prolamins initiate an inflammatory response when they reach the small bowel enterocyte. CeD, which can only occur in genetically predisposed individuals (HLA DQ2 or DQ8), is an underrecognized entity with many nutritional considerations. The estimated prevalence is 1% worldwide, though it is has classically been underdiagnosed due to its wide range of presenting symptoms and underrecognition.[1] The prevalence of CeD has increased fivefold in the last 50 years with various hypotheses

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Division of Gastroenterology, Hepatology, and Nutrition, Center for Nutrition, Vanderbilt University Medical Center, 1211 21st Avenue South, Suite 514, Nashville, TN 37232, USA
* Corresponding author. Division of Gastroenterology, Hepatology, and Nutrition, Vanderbilt University Medical Center, 1211 21st Avenue South, Suite 514, Nashville, TN 37232.
E-mail address: Dawn.W.Adams@vanderbilt.edu

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including the hygiene hypothesis and possible infection by reovirus at an early age.[2,3] CeD has important long-term health concerns, such as the increase in osteoporosis, depression, non-Hodgkin lymphoma, and small intestinal adenocarcinoma. Nutrient deficiencies are common, such as vitamin B12, folate, B6, iron, vitamin D, magnesium, copper, and zinc. It is important to perform monitoring of these in patients with CeD.

Some patients without CeD report having a sensitivity to gluten, a condition called nonceliac gluten sensitivity (NCGS) or nonceliac wheat sensitivity (NCWS). Though a biological basis has yet to be determined, there may be an immune response, which is distinctly different from that seen in CeD.

This article briefly reviews the pathogenesis and symptoms of CeD and NCGS and, in more detail, discusses the nutritional complications seen in CeD before and during treatment, and the nutritional consequences of a long-term gluten-free diet (GFD).

GLUTEN

Gluten is derived from the Latin word for glue due to its viscoelastic properties. Gluten is the material that remains after washing away starch and water soluble components of wheat dough. Gluten mainly consists of a group of proteins called prolamins, primarily soluble gliadins and insoluble glutenins. The properties of gluten can best be demonstrated during dough mixing in which dough stiffness increases due to optimization of these protein interactions.[4] Because of this, gluten is a common additive in many food products that are naturally devoid of gluten to optimize texture and storage properties, and is a large component of the food industry.[5]

Gluten is naturally found in wheat, rye, and barley. However, a GFD must eliminate all sources of gluten, which includes any foods or products that have added gluten. This can include anything from salad dressing to cheese to medications. Pure oats are devoid of gluten but the processing of oats with gluten-containing grains has caused many people to eliminate oats as part of a GFD (see later discussion). Gluten itself has little nutritional value; however, foods naturally containing gluten are a common source of whole grains, fiber, vitamins, and minerals.

CELIAC DISEASE

CeD involves a complex interplay of genetics, immunologic factors, and gluten (**Fig. 1**). The basis for treatment of CeD is avoidance of gluten, therefore it excludes wheat, barley, and rye.[6] Gluten and other proline-rich proteins are poorly digested in the small intestine due to lack of prolyl endopeptidases, resulting in large gluten proteins. Moreover, gluten is rich in glutamine which can be deamidated by the enzyme tissue transglutaminase and converted to negatively charged glutamic acid residues.[7] Some of these peptides can bind to human HLA class II molecules DQ2 and DQ8, which activate $CD4^+$ T cells in the intestinal mucosa. This leads to a T-cell–mediated response to gluten in genetically susceptible individuals, resulting in a malabsorptive enteropathy.[8] The humoral immune system is directed against the exogenous antigen gluten and the autoantigen tissue transglutaminase. Disease is exhibited through a complex interplay of the mucosal and epithelial barriers via the disruptions and alterations of intestinal epithelial cells and tight junction defects.[8,9] Histologically, this leads to intraepithelial lymphocytosis, crypt hyperplasia, and villous atrophy, which are the hallmarks of biopsy diagnosis.[10] A strict GFD can lead to mucosal healing, resulting in improvement in histologic findings, malabsorption, and symptoms.

CeD can present with a wide array of symptoms. The classic presentation was a thin child with weight loss, poor growth, and diarrhea. Now patients are presenting with more atypical symptoms (**Table 1**).[11] Given the high frequency of many of these symptoms in