Is 'Gluten-Free' Gluten-Free? Celiac Disease in Canada in 2015

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About the Authors

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Summary

Our understanding of celiac disease (CD) has improved dramatically in recent years. Once considered a rare childhood malabsorption syndrome, we now recognize CD as a complex enteropathy mediated by immune, genetic, and environmental factors. CD affects a large proportion of the Canadian population, and its disease burden is substantial in terms of proven reduction in quality of life. Symptom recognition and referral to a gastroenterologist for diagnosis are crucial. As CD is caused by intolerance to gluten, the only effective treatment is strict gluten avoidance. Canadian food product guidelines have only recently become sufficiently rigid, incorporating newer evidence that suggests lower limits of gluten tolerability in this patient population than previously thought.

Résumé

Dans les dernières années, nous en avons appris énormément sur la maladie coeliaque. Il fut un temps où nous pensions qu'il s'agissait d'un syndrome de malabsorption infantile rare, mais nous savons désormais que la maladie coeliaque est une entéropathie complexe où entrent en jeu des facteurs immunitaires, génétiques et environnementaux. La maladie touche une grande proportion de la population canadienne et a des répercussions considérables sur la qualité de vie. La détection des symptômes et l'aiguillage du patient en gastroentérologie en vue de l'établissement du diagnostic sont des éléments cruciaux de la prise en charge. Étant donné que la maladie provient d'une intolérance au gluten, le régime alimentaire strict sans gluten constitue le seul traitement efficace. Ce n'est que récemment que les lignes directrices canadiennes sur les produits alimentaires ont été resserrées à la lumière de nouvelles données probantes indiquant que la tolérabilité au gluten dans ce groupe de patients est moindre que ce que l'on pensait auparavant.

Background and Pathogenesis

Gluten, a composite protein found in wheat (as well as in the related species barley and rye), is responsible for the histopathologic and clinical changes observed in celiac disease. The degree to which oats may be contaminated with gluten and whether they are safe for consumption by CD patients are issues currently being studied.¹⁻³ At any rate, a diet intentionally lacking in gluten — a gluten-free diet — has become established as the standard therapy for CD patients; adhering to a gluten-free diet has consistently been shown to induce remission in this population.⁴ The exact pathogenesis of CD is not fully understood, but there appears to be an interplay between immune, genetic, and environmental factors.

Canadian Epidemiology

CD continues to be under-diagnosed, yet prevalence is nevertheless high, at approximately 1% of the population.^{5,6} The national case load, according to the Canadian Digestive Health Foundation, lies between 110,000 and 330,000.⁷ This range represents the disparity between the population currently labelled with CD (and managed accordingly) and the proportion that remains undiagnosed. Rates of CD have roughly doubled in the Western world in the last 25 years. This comes primarily as a result of heightened clinical suspicion and improvements in diagnosis.

Clinical Presentation and Disease Burden

The clinical spectrum of CD is vast. It comprises gastrointestinal symptoms of varying severity (diarrhea, bloating, abdominal pain, constipation, and weight loss, among others) as well as several extraluminal presentations. These include anemia, dermatitis herpetiformis (pruritic papulovesicular eruptions most commonly found on extensor surfaces), arthralgia, dysmenorrhea, neuropathy, and osteopenia, among others. The most severe process connected with untreated CD is enteropathy-associated T-cell lymphoma (EATL).⁸ There are also well-known associations between CD and endocrine conditions, such as insulin-dependent diabetes, thyroid dysfunction, and adrenal insufficiency. As with other immune conditions, there appear to be higher rates of CD in the female population, although this may partially be due to a higher incidence of osteoporosis and anemia in this population, which leads to increased diagnosis of CD.⁹ There should be increased clinical suspicion for patients with a documented family history of CD.

There is a substantial reduction in quality of life associated with a diagnosis of celiac disease. Observing a gluten-free regimen is challenging by any account, both for economic and personal reasons. In a recently published cohort study, 73% of CD patients avoided dining outside of their homes at least some of the time, while 78% reported feeling left out of social functions at least some of the time. Strikingly, 81% stated they had difficulty purchasing gluten-free foods at least some of the time. Perhaps most importantly, a staggering 93% of CD patients described at least some difficulty determining whether a particular food was truly gluten-free.¹⁰ Thus one can imagine that CD takes its toll on patients not only via direct symptoms, but also indirectly on quality of life. The same study demonstrated that 47% of CD sufferers feel depressed at least some of the time as a result of their disease. Meanwhile, 53% described alterations in their social activity because of CD, and only 37% described feeling energetic all or most of the time.¹⁰

Diagnosis and Management

Diagnosing CD can be challenging by virtue of its broad clinical presentation. Not all CD patients will present with gastrointestinal symptoms, and there are patients who have histopathologic changes and mild to absent symptoms, leading to under-diagnosis. The gold standard of diagnosis remains histologic sampling via small bowel biopsy. However, there is a role for serologic testing in patients in whom there is appropriate clinical suspicion of CD. A recent well-designed systematic review evaluated the properties of blood tests readily available to primary care practitioners.¹¹ IgA

anti-tissue transglutaminase (IgA-tTG) was shown to have a pooled sensitivity of 89% and a specificity of 98%. A second serological marker, IgA anti-endomysial antibodies (EmA), had a pooled sensitivity of 90% with a specificity of 99%. Other serology and clinical symptoms were found to be less helpful in establishing diagnosis.

CD serology is expensive and often comes at personal cost to the patient, depending on the laboratory. Referral to a gastroenterologist should be made if the diagnosis is being considered. IgA deficiency can affect test results, and therefore, quantitative immunoglobulin measurement should also be performed for patients in whom clinical suspicion exists. As mentioned, endoscopic biopsy of the small bowel, coupled with clinical and histologic remission on a gluten-free diet, remain the definitive diagnostic parameters. A gluten-free diet is the only means of achieving remission in CD, and compliance is difficult due to the socioeconomic and personal issues listed above. A recent Canadian study found that gluten-free products, on average, were 242% more expensive than their equivalent gluten-containing counterparts.⁷

Defining a Safe Gluten Threshold in 2015

Importantly, the amount of daily gluten intake that CD patients are able to tolerate varies considerably within the population. The so-called gluten threshold, or lower limit of daily exposure that results in pathology and/or symptoms, therefore becomes important to establish. The gluten threshold is a patient-specific value that represents the maximum allowable daily consumption of the protein and is generally represented by the unit mg per day (gluten content of specific foodstuffs is denoted by parts per million [ppm or mg/kg], a value that can then be translated into mg/day by approximating the average daily intake of CD patients). There is an area of research concerned with the subset of patients for whom even a so-called “gluten-free diet” may be contaminated with enough gluten to cause symptoms or histopathologic change.¹²

Several studies have sought to define a safe gluten threshold for CD patients; these have been summarized in two recent systematic reviews.^{13,14} Unfortunately, these studies are heterogeneous in terms of study design, patient age, exposures, measurement techniques, and outcomes. These factors prevented the data from being meta-analyzed in any meaningful way. Despite this, best current evidence suggests that consumption of even small amounts of gluten (between 10 and 50 mg daily) is sufficient to reproduce symptoms as well as induce villous change in most CD patients. These thresholds are primarily driven by arguably the most robust study available, a randomized trial performed in 2007.¹⁵ If one

uses an average consumption of gluten-free foods of 300–500 g per day for CD patients (a typical range in most European and North American countries), one calculates an allowable upper limit for gluten in gluten-free foods of 20 ppm (or mg/kg). The method that has been studied and validated most extensively in gluten quantification is the enzyme-linked immunosorbent assay (ELISA), several subtypes of which exist.¹⁶

Despite these data, industrial and governmental standards for gluten content vary substantially among countries. In 2008, the World Health Organization (WHO) and Food and Agriculture Organization (FAO) offered an updated version of the Codex Alimentarius, proposing that 20 ppm should be the maximum allowable ratio of gluten for a product to be labelled “gluten-free.”¹⁷ Up until recently, however, the Canadian Celiac Association (CCA) stated simply that “gluten-free in Canada means that the food does not contain wheat, spelt, kamut, rye, barley, oats, or triticale, or any parts thereof.”¹⁸

Fortunately, 2012 marked the start of a new era of food labelling in Canada, with important changes made to national labelling regulations. As a result, “labels for all food products sold in Canada will have to carry clear identification of the priority allergens, gluten, and added sulphites at a level greater than 10 ppm.”¹⁸ Health Canada has stated that “industry has been given 18 months to implement the new allergen labelling regulations” (from August 2012).¹⁹ This legislation is crucial in striving to improve quality of life and disease burden from CD nationwide. In addition, CCA has also unveiled an innovative Gluten-Free Certification Program (GFCP). This initiative will allow industrial facilities to apply to be branded with the CCA/GFCP logo after several quality control standards are met, again providing confidence to consumers.²⁰

Conclusion

There is substantial disease burden associated with CD. Primary care physicians and specialists alike must maintain a high degree of clinical suspicion for this disease and employ early referral to a gastroenterologist for formal diagnosis. Adhering to a strict gluten-free diet is the only known treatment for CD, and historically, this way of life has been difficult, as well as potentially misleading, for consumers. Armed with new labelling directives, the GFCP initiative, expanding arrays of gluten-free products, and advanced techniques in diagnosis, Canadians with CD should now be recognized and protected, as they should. As Canadians in 2015, we proudly lead by example in being able to accurately label our gluten-free products “gluten-free.”

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