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Perspective: Gluten-Free Products for Patients with Celiac Disease Should Not Contain Trace Levels[1–3]

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Introduction

Celiac disease (CD)[10] is widely defined as an autoimmune disease triggered by the consumption of dietary gluten in genetically predisposed individuals. It is now well documented that a strict gluten-free diet (GFD) for life is the only method currently available to treat and prevent CD complications (1). Present evidence strongly suggests that a GFD protects patients with CD from complications of untreated disease, including malignant lymphoma. In addition, other extraintestinal symptoms and complications may occur (2). The current European Commission (EC) regulation 41/2009 states that the removal of gluten from gluten-containing grains presents difficulties and economic constraints so that the manufacture of totally gluten-free food is difficult (3). Moreover, some foods on the market contain residual gluten. Despite this information, foods are often labeled as "gluten-free" but may contain gluten to a maximum of 20 mg/kg or as "very low gluten" (up to a maximum to 100 mg/kg). For a more global approach and to permit comparison with North America, the use of alternative labeling has been suggested as follows: <20 ppm or <100 ppm, respectively. Essentially, these labels could be misleading to some with CD, especially if the foods consumed are thought to be gluten-free but are not. Gluten consumption in patients with CD may cause profound symptoms and marked inflammatory changes in the small intestine, or the development of other associated diseases. Others may have few symptoms despite consumption of trace amounts of dietary gluten, and yet a serious and persistent immune reaction to trace amounts of gluten may still occur. In the EC, it is also noted that "most but not all people with intolerance to gluten can include oats in their diet without [an] adverse effect on their health" (3). This statement is inaccurate because there are many varieties of oats and oats should be included in a GFD only if shown to be free of gluten. Some varieties of oats probably induce an immune response, and several research studies have shown harm caused by oats in the CD diet (4, 5). In part, this may reflect the contamination of oats by other grains, possibly during processing. Current legislation may be understood to represent a compromise between the technological capabilities of food production and the actual requirements of patients with CD. In any case, the current EC regulation markedly affects the entire European food market and may have a significant impact on the lives and health of patients with CD. We believe that a robust discussion involving different professionals in this field is needed. Knowledge related to food labeling, specifically on the gluten content of different foods, is inadequate, not only for patients suffering from CD but also on the part of professionals involved in their medical care. Last, the reaction to gluten varies greatly among patients with CD and many will not manifest symptoms, although the immune-mediated inflammatory process persists. Some patients without proper treatment will remain clinically unwell or experience relapse. The main objective here is to recommend a new classification for food labeling and to suggest that gluten-free products contain no gluten.

Suggestion for New Classification

The designation "gluten-free" should be used to label foods that are known to be entirely free of all gluten-containing products. Food products recommended for patients with CD should have "0 mg/kg"—that is, they should contain no gluten. "Very low gluten" foods may have a low gluten

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[10] Abbreviations used: CD, celiac disease; EC, European Commission; GFD, gluten-free diet; HLA, human leukocyte antigen.

concentration, perhaps 100 mg/kg (or <100 ppm). These products are specifically not recommended for patients with CD and this should be noted on the product label. Oats should be included in a GFD only if the product has been tested and shown to be free of gluten. If the oat products are not tested, this information should be included on the label.

Independent studies show that the prevalence of CD in Europe ranges from ~1:100, with differences between some countries (6). In the United States, the expected prevalence is from 1 in 111 to 1 in 141 patients (7, 8). Indeed, we know that most patients with CD have not been detected (9, 10).

The basis of GFD legislative actions and our suggestions

Over the past year, there has been a global increase in the diagnosis of CD in children and adults. Indeed, current data confirm the original assumptions of some experts that there is a higher prevalence of CD than previously thought (11). Therefore, it can be anticipated that large numbers of patients with CD will require a GFD. It is also known that gluten-related disorders have received much attention in the popular press and the sale of foods labeled as gluten-free has become a multibillion dollar business (12). These trends are based mainly on some current findings on the impact of dietary gluten on human health. A great deal of effort has been devoted to the evaluation of the adverse effects of gluten on healthy populations, perhaps more than necessary. In contrast, only limited effort has been devoted to the use of natural alternatives to gluten-containing foods. It seems that GFD are based more on profit than on health. The recommendation of <20 ppm gluten for a GFD was originally based on a study in only 49 adults with biopsy-proven CD who were treated with a GFD (13). The results showed that the ingestion of contaminated gluten should be kept at <50 mg in the treatment of CD. Currently, a concentration of 20 ppm is widely accepted as safe and is the international standard adopted as part of the Codex Alimentarius and implemented in the European Union (14). However, other studies have documented that even a minimal amount of gluten may be dangerous for persons suffering from CD. In some, gluten may trigger an immediate immunologic reaction with variable degrees of small intestinal inflammatory changes (15, 16). It is therefore probable that some consumers may rapidly feel the negative effects of residual amounts of gluten. Our laboratory, along with experience from clinical practice, has found that many patients complain of gastrointestinal problems after consuming some "gluten-free" products. Today, some producers have certified laboratories to assess the gluten content of their products. In a prospective study (17), most of the products tested contained <20 ppm gluten, which is less than the permitted amount of gluten. Others have also hypothesized that CD can develop in any decade of life (18). This may result from a combination of several factors such as high gluten content, genes [human leukocyte antigen (HLA) alleles], and triggers such as stress, pregnancy, illness, menopause, antibiotic use, gastrointestinal infections, or viruses that ultimately lead to immunologic reactions to gluten (19, 20). This may be temporary or persist for a lifetime (21). However, we believe that even trace amounts of gluten have a negative impact on the health of patients with CD, regardless of age. From a nutritional perspective, a widely varied diet is important to encourage consumers to utilize foods that are completely free of gluten (22).

Oats in a GFD diet

Oats are considered to be a cereal, and some studies have shown that oats may provoke a reaction similar to gluten-containing grains; however, some have also suggested that uncontaminated oats are well tolerated by most people with CD (23), even over the long term (24). Tjelström et al. (25) showed that oats affect the function of the gut microflora, and some children with CD who consume oats may develop gut mucosal inflammation and, as a result, are placed at increased risk of future disease complications. Interestingly, Silano et al. (26) found significant differences among oat cultivars in eliciting the transglutaminase-2-mediated events of CD inflammation. The North American Society for the Study of CD has released a statement seeking to clarify their position on oats as a gluten-free food. Most experts agree that oats that are uncontaminated by wheat, barley, and rye can be safely consumed by most people with CD (27, 28). However, we believe that only manufacturers that use strictly gluten-free oats can state that their product is gluten-free. In our view, the avoidance of oats in patients with CD remains controversial, but those who consume foods containing oats should be carefully monitored until there is more evidence to show the safety of oats and varieties of low-toxicity oats (29). Until there is strong evidence that a particular variety of oats is gluten-free, it is not possible to state that oats is a gluten-free food. Some have suggested that patients with CD should only add oats to their diet if established with a conventional gluten-free diet, and cease oats ingestion if symptoms develop (30). It is also recommended that individuals with CD have both initial and long-term assessments by a health professional when introducing pure oats into a GFD (31). These data support our suggestion that all oats-containing foods should not be part of a GFD.

Conclusions

Although it may be difficult for manufacturers of gluten-free foods to ensure gluten-free products, this is essential for the long-term health of individuals with CD. The current EC legislation is essentially based on an assumption that patients with CD can consume minimum amounts of gluten. However, this is not possible without an increased risk of recurrent or persistent symptoms, ongoing small intestinal inflammatory change, and the need to monitor and treat long-term consequences of inadequately treated CD. Thus, the term "gluten-free" on food labeling should be reserved for products without any detectable gluten. "Very low gluten" foods may have a minimal gluten concentration, perhaps <100 ppm, but they are not recommended for patients

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