NUTRITIONAL RECOMMENDATIONS FOR CELIAC DISEASE

Nutrition 303, Canadian College of Naturopathic Medicine

Abstract

Celiac disease simply put is an intolerance to the protein gliadin, more commonly known as gluten. The current recommendation is complete avoidance of gluten proteins. However, this can be difficult for patients to achieve without guidance. This inquiry will explore the mechanism of action, the specific nutrients which may be deficient in celiac disease, and patient resources for healthy gluten free meals and recipes.

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Inquiry

In the recent years, the prevalence of celiac disease (CD) has increased in Canada and in North America. CD average prevalence in western countries is approximately 1% of the population. It is estimated that there are 16,540 Canadian children younger than 5 with celiac disease; however, this data is based upon a conservative estimate from other western countries at a 0.9% incidence rate (Fedorak, Switzer & Bridges, 2012). The rate of CD seems to be rising, which may be explained by rates of detection of CD are increasing, especially in atypical cases (Lamireau & Clouzeau, 2013). There is a substantial prevalence of celiac disease that is asymptomatic and may not be detected. A delay in the diagnosis of celiac disease leads to complications such as "chronic gastrointestinal complaints, refractory iron-deficiency anemia; infertility; osteoporosis; intestinal lymphoma; and, possibly, the development of other autoimmune diseases (eg, type 1 diabetes)" (Fedorak et al, 2012). The mortality rate due to celiac disease is approximately 7 individuals per year (Fedorak et al, 2012). However, the prognosis is good if a strict gluten free diet is followed. In fact, 95% of people who adhere to a gluten-free diet notice improvement of symptoms in days to weeks (Fedorak et al, 2012).

Mechanism of Action

Celiac disease is a result of a genetic abnormal immune reaction to a gliadin, or gluten, protein which activates the immune system (Martucciello, Paolella, Esposito, Lepretti, & Caputo, 2018). Hallmarks of celiac disease include auto-antibodies to enzyme type-2 transglutaminase (TG2) and intestinal mucosal atrophy and hyperplasia (Martiucciello et al, 2018). Specifically, there is presence of villous atrophy and lengthening of the intestinal crypts (Frank, 2018). The intestinal mucosa is compromised by the presence of any amount of gluten protein in the diet: a deamidation reaction of glutamines from gluten-derived gliadin peptides is enhanced by TG2 for increased immunogenicity (Martiucciello et al, 2018). The presence of these HLA class 2 DQ2 or DQ8 molecules "activate CD4 T cells in the intestinal mucosa" (Pelkowski & Viera, 2014). This causes chronic inflammation in the small intestine, leading to malabsorption (Pelkowski & Viera, 2014). Further, TG2 may itself cross link and form TG2-gliadin complexes which cause an auto-immunogenic response via hapten-like antigen presentation (Martiucciello et al, 2018). These anti-TG2 antibodies are found in the intestinal mucosa as well as throughout the serum in celiac disease patients (Martiucciello et al, 2018). The mutation of antibodies for the anti-TG2 present in the serum may be a reason for which there is an increase in incidence of other auto-immune diseases and dysregulation.

Another hypothesis of the mechanism is that in response to gluten there is a non-proliferative activation of lamina propria CD4+ lymphocytes, while a proliferative activation of "intra-epithelial TcR alpha/beta CD8+ and TcR gamma/delta lymphocytes" is concurrently present (Muller et al, 2005). It has also been postulated that T lymphocytes are not the only immune cells involved but there is a synergistic effect of B lymphocytes, natural killer (NK) cells, neutrophils, eosinophils, macrophages and mastocytes but their role has not been clearly established (Muller et al, 2005).

There are several forms of celiac disease including: active CD, silent CD, and latent CD (Martiucciello et al, 2018). Active CD is an active autoimmune dysregulation in the presence of gluten with abnormal antibody results gastrointestinal symptoms, and histological changes to the villi; latent CD may have the presence of abnormal antibodies or genes but no histopathologic evidence of damage (Martiucciello et al, 2018) Latent celiac disease may have immunological abnormalities such as "as increased count of IELs (particularly gamma-delta T cells, Marsh type-1) and positive EMA or tTG-antibody tests are sometimes present" and these individuals may develop clinically active CD later in life (Holtmeier & Caspary, 2006). Silent CD includes a histopathological abnormality, such as the loss of villi, and may have abnormal antibody or genetic results, but have no symptoms of the condition. With time, there is a typical progression from latent CD to silent CD, and then to the active disease. If a strict gluten free diet is followed, there is a regression from active CD to the latent form of CD (Lamireau et al. 2013).

Diagnostic Strategy

The standard of determining celiac diseases consists of: physical exam, immunoglobulin A tissue transglutaminase serologic test, and biopsy of the small intestine to confirm diagnosis of celiac disease (Pelkowski & Viera, 2014). There are many choices of serologic tests for CD. IgG deaminated gliadin peptide is specific at 98% a for celiac disease with an LR positive of 40 and an LR negative of 0.02 as is a good option for serologic testing for celiac disease (Fedorak et al, 2012). However, the IgA tissue transglutaminase (IgA tTG) tests with a specificity of 95 and LR positive of 17.5 and negative 0.04. In terms of effectiveness and cost, IgA tTG is the gold standard for serologic diagnosis and monitoring of CD (Fedorak et al, 2012). Although approximately 90% of celiac disease patients carry the HLA DQ2 allele, routine testing is not recommended (Elsevier Point of Care, 2018). It is important to perform these tests prior to the restriction of gluten in the diet to avoid false negative results.

It is important to note that villous atrophy is not unique to celiac disease but present in a variety of conditions including: immunodeficiency, Crohn's disease, giardiasis, HIV, intestinal lymphoma, tuberculosis, Zolliger-Ellison syndrome among others (Pelkowski & Viera, 2014). In this way, we must be sure to do our due diligence and refer for adequate testing where appropriate. As well, the following are considered to rule out associated co-morbitides and deficiencies: iron/ferritin, B12 for

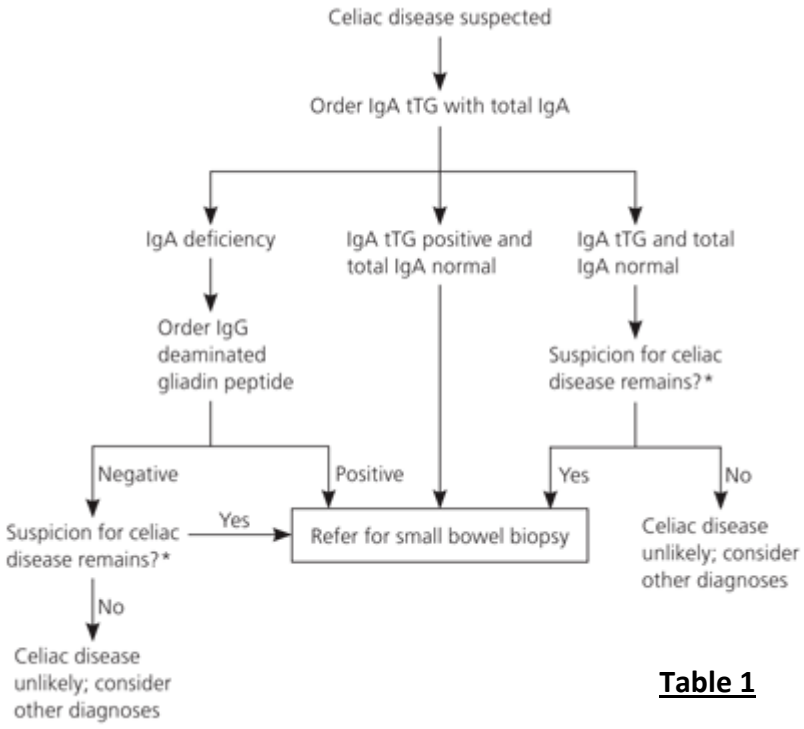

Table 1

anemia, edema for hypoproteinemia, signs of peripheral neuropathy or ataxia (Elsevier Point of Care, 2018). Included is an algorithm which highlights the standards of care from American Family Physician (Pelkowski & Viera, 2014). See Table 1

Nutrient Supplementation

Celiac disease causes a significant amount of malabsorption. This malabsorption may lead to numerous deficiencies including: low levels of iron, fat-soluble vitamins, vitamin B_{12}, and folic acid (Elsevier Point of Care, 2018). As malabsorption is a prominent issue, especially with delayed diagnosis, patients should be advised to consume a multiple vitamin and mineral supplement, which contains "vitamin A, D, E, Folic acid, B-6, calcium, copper, iron, magnesium, selenium and zinc" to correct deficiencies (Prousky, 2012). Supplemental Vitamin D may be beneficial, especially in secondary hyperparathyroidism at 1000-4000IU per day (Prousky, 2012). Vitamin E may be of use especially in cases of sensory loss, ataxia and retinitis pigmentosa at 300- 3000 IU per day for 6 weeks and then a maintenance dose of 400-800 IU per day (Prousky, 2012). Vitamin K may be depleted, and there may be a tendency of increased bleeding time or PT which may also impact "hemoglobin levels, iron levels, proteins, cholesterol and serum aspartate transaminase" as well as gastrointestinal manifestations, low bone mineral density and weight loss (Prousky, 2012). A dose of 10 mg of vitamin K intramuscularly is recommended (Prousky, 2012). Calcium levels must be supplemented at 1200-1500 mg per day to prevent osteoporosis or osteopenia due to malabsorption (Prousky, 2012). Carnitine may be considered especially in cases of fatigue, a non-specific symptom of CD. Carnitine allows for amino acids to be transported into the mitochondria; therefore, increases cellular energy. A dose of 2000 mg per day would help with this transport and decrease levels of fatigue as well as decrease risk for encephalopathy and cardiomyopathy in CD patients (Prousky, 2012). Finally, after serology is performed if anemia is present a supplementation of iron, folate, and B-12 should be administered if there is deficiency, especially if there is ileal involvement as indicated on biopsy (Frank, 2018).

Diet Strategy

The proposed diet is strict adherence to a gluten free diet. The diet plan provided is based upon a Mediterranean style eating plan rich in vegetables, fruits, fish, lean protein, and olive oil while minimizing sweets, and processed foods. A Mediterranean style diet has been chosen for its affinity for cardiovascular parameters, diabetes, and anti-inflammatory properties. The Mediterranean diet has also been shown to decreases the rates of obesity and cancers including colorectal and breast cancers which are relevant to the celiac disease population where weight gain and a 30% increased risk of cancer are often comorbidities (Widmer, Flammer, Lerman LO, Lerman A, 2015).

See the patient handout, appendix A.

Anticipated Challenges

There are some anticipated challenges with switching to a gluten free diet. Particularly, if the patient's current diet is the standard American diet. Dietary changes and eating can be a major social hurdle and can change relationships with family, friends, and during social outings. Gluten containing foods may be a part of cultural foods and social gatherings which may be a deterrent in adherence. The standard American diet, and the Canadian food guide recommend a large portion of grain foods including wheat, which may be confusing for patients. Another important consideration is the cost of a gluten free diet. The average costs of the gluten-free items were 242% more expensive than their gluten-containing counterparts (Fedorak, 2012). For patients with lower socioeconomic status, there may be a barrier in purchasing nutritious gluten free foods. There are government subsidy programs that can be utilized from the government of Canada, but this subsidy is only applicable to specific gluten free foods such as gluten free breads, pastries, etc. These are not necessarily healthy foods to be consuming. Further, the subsidies do not apply to non-gluten containing foods such as increased fruits and vegetables and gluten free whole grains that are not packaged. Further, if several people in the household adopt a gluten free lifestyle, the subsidy only applies to the individuals with celiac disease; therefore, only a portion of the foods are eligible for reimbursement (Canada Revenue Agency, 2018).

Another challenge may be in identifying hidden sources of gluten in seemingly safe foods. For example, soya sauce, sauces, spice mixes, and condiments often contain hidden gluten. In addition, there also may be cross contamination of foods that people with celiac disease must be weary of including home cooked meals as well as when going out to restaurants. In restaurants there may be residual gluten in fryers, pans which will cause an exacerbation of symptoms in a celiac person. People with celiac disease may experience embarrassment or perceived nuisance when advising restaurant staff about their health condition which may lead to social isolation. There may be issues of compliance because of weight gain after following a gluten free diet. In fact, "in an American study (n=188), after two years on a gluten-free diet, 81% of patients experienced weight gain [:] for patients who were overweight at baseline, 82% gained additional weight" (Fedorak, 2012).

In order to overcome these challenges, it is important to give the information to patients and collaborate to find solutions to anticipated challenges. Primary care physicians should take the time to explain a gluten free diet with their patients and emphasize that it is of utmost necessity for their health. Physicians should also emphasize the importance of adherence to the diet for symptom relief which may increase compliance. Further, non-adherence and cancer risk should be highlighted "patients have a 30% increased risk for developing a malignancy compared with the general population; the most common is non-Hodgkin's lymphoma" (Fedorak, 2012).

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