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Expert Opinions

Gluten-Free Diet and Migraine

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Migraine is common in celiac disease (CD) and usually improves on a gluten-free diet (GFD). The benefit for people impacted by migraine without CD is poorly evidenced. A GFD may have adverse health consequences and is expensive.

Key words: migraine, gluten-free diet, celiac disease, gluten sensitivity

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The interaction between diet and health is certainly not a new concept. The role of gluten and its effects can be dated back to the first century AD. In the 1940s, Dutch physicians appreciated symptomatic improvement within the pediatric celiac disease (CD) population when reducing wheat and rye.[1] Certainly, the gluten-free diet (GFD) has increased its presence within popular culture in more recent years with broad sweeping claims without sound supporting scientific evidence.[2]

CASE 1

This 33-year-old female is seen with a history of chronic migraine since her teens. She also has depression, anxiety, frequent episodes of diarrhea, and fatigue.

CASE 2

This 40-year-old female has a 10-year history of episodic migraine. She also has a history since her teens of alternating diarrhea and constipation. The gastroenterologist performed testing which was negative for CD and she was diagnosed with irritable bowel syndrome. After reading on social media, she went on a GFD and reported that her migraines were less frequent.

QUESTIONS

Is there an association between CD and migraine?
Which patients impacted by migraine should be screened for CD and how?
Does migraine improve after going on a GFD?
Does a GFD improve migraine in those without CD?
Is there any harm to a GFD?

Celiac Disease and Migraine.—The association between headache, specifically migraine, and gluten has been best documented in patients with CD. Chronic migraine was found to be twice as frequent in patients with CD and gluten sensitivity compared to controls.[3] In a large, meta-analysis performed by Zis et al, the estimated prevalence of headache in adults with CD was noted to be 26%; several case reports noted headache being the initial presenting symptom of these patients. After adopting a GFD, up to 75% of patients with CD saw improvement in headache.[4] Lionetti et al demonstrated the beneficial effect of a GFD in CD with a reduction in headache frequency in the

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majority of patients and noted 27% of patients became headache-free.[5] In another study of 866 subjects who reported headache, tension-type or migraine, as the main symptom of CD, subjects with migraine who initiated and followed a GFD had greater improvement in the frequency and severity of their headache much more than those with tension-type headache.[6] Limitations of these cited studies arise from variations in diagnostic criteria and the difficulty in differentiating tension-type headache and migraine.[5]

Which People Impacted by Migraine Should Be Screened for CD and How?.—The presentation of CD classically includes diarrhea, bulky, foul-smelling, floating stools due to steatorrhea, and flatulence.[7] However, a myriad of both intra- and extraintestinal symptoms have been reported. Specifically reported neurologic symptoms include dementia/amnesia/cognitive deficits, ataxia, epilepsy, chronic neuropathies, personality changes, headaches, and cases of associated neuromyelitis optica, muscular hypotonia, and delayed motor development.[8]

As with most conditions in medicine, there is believed to be a combination of inheritance and environment.[2] There is a 20% chance of inheritance of CD from first degree relatives and current theories also include timing of gluten introduction, cesarean delivery, lack of breastfeeding, recurrent childhood GI infections, and host microbiome.[9] Obtaining a family history of dietary conditions for people impacted by migraine is useful for a comprehensive work up.

Patients with migraine who experience any celiac symptoms should be referred for testing. Testing is usually best initially through tissue transglutaminase IgA antibody (tTG-IgA: 98% sensitivity; 95% specificity) while the patient is on a gluten-containing diet.[10] The only confirmed method of diagnosis is with an intestinal biopsy consistent with crypt hyperplasia with a decreased villi/crypt ratio as well as blunted or atrophic villi.[10] Aside from the standard barriers in obtaining semi-invasive diagnostic testing, the requirement to be on a gluten-containing diet can also restrict patients to get disease confirmation. For most children and adults, the best way to test for CD is with the tTG-IgA, plus an IgA antibody in order to ensure that the patient generates enough of this antibody to render the CD test accurate.

Does Migraine Improve After Going On a GFD?.—A study found that approximately 95% of patients who follow a GFD show clinical improvement within days to weeks. However, patient compliance with dietary treatment is difficult.[11] Failure of IgA tTG titers to decrease in about 6 months suggests continued ingestion of gluten. Patients and families may need frequent dietary education and assessment of compliance.[11] Support groups could be helpful with diet maintenance. Repeat endoscopies are not routinely needed, but antibodies can be followed every 3-6 months until normalization. If antibody levels have increased after 6-12 months of adequate dietary treatment, repeat biopsies should be considered.[10]

Does a GFD Improve Migraine in those Without Celiac Disease?.—In consideration of reactions to foods, it is noteworthy to delineate the differing responses (ie, allergy vs intolerance or sensitivity). This distinction can be beneficial in counseling patients as the former is typically more harmful than the latter. Sensitivities generally result in a less severe symptomology, and therefore, may not require strict avoidance. The most common recognized intolerance to gluten includes CD, non-celiac gluten sensitivity (NCGS), and a specific wheat allergy. A specific wheat allergy is a hypersensitivity reaction to wheat protein that results in mast cell activation and an immune response, both IgE and non-IgE. Unfortunately, there is a paucity of data regarding NCGS and headache. One cohort study of 486 patients, both children and adults, showed a possible association with 54% of patients noting prevalence of headaches.[11] Challenges arise in attempting to study gluten sensitivities with headache association due to limitations in making a diagnosis of NCGS, confounding factors in diet modification, difficulty in studying patients who may elect to stay on a GFD instead of receiving further diagnostic confirmation, and overlap with similar conditions such as irritable bowel syndrome.[12] Evidence of the benefit of a GFD is unclear at the present time and may have unforeseen health and financial ramifications of which patients should be aware and counseled.

Is there Any Harm to a GFD.—The GFD primarily consists of fruit, vegetables, seafood, meat, poultry, legumes, nuts, and most dairy products. Frequently glu-

ten alternatives consist of rice, corn, quinoa, millet, and amaranth.[13] As the diet has increased in popularity, it is important to understand the potential health and financial impact it may have on patients.

An evaluation by Dunn et al revealed that 31% of participants believed gluten avoidance would promote general health and 37% felt that gluten-free products were healthier than their conventional equivalents;[14] however, gluten-free products were found to be lower in fiber, iron, B vitamins, calcium, vitamin D, phosphorus, and zinc.[2] Additionally, gluten-free substitutes tend to contain a higher amount of calories from fat with more carbohydrates and a higher glycemic index,[15] and the sodium content is often higher than equivalent products.[16] After the decision has been made to adapt a GFD, the discussion of gluten-free products and their content should be discussed between a dietician and the patient regarding taking caution on the inadequate nutritional value.

In a study of 679 patients with confirmed CD and confirmed adherence to a GFD by a dietician, the mean body mass index (BMI) increased significantly after the initiation of a GFD. This is concerning to the migraine population who also have CD or NCGS who adapt a GFD, because an increased BMI can contribute to an increase in frequency or increase in severity of migraine pain.[17] Additionally, patients with increased BMI may experience more severe associated migraine symptoms of disability, photophobia, and phonophobia.[18] Patients with existing obesity or at risk for obesity with a diagnosis of CD may require further counseling of behavior weight loss in addition to the adoption of a GFD.[19] Patients with NCGS who experience migraine may benefit from working with a dietician, nutritionist, or gastroenterologist.

Aside from the differences in nutritional content, the cost of gluten-free products is often greater. Although the greater demand for gluten-free products has resulted in more options, gluten-free foods can cost 200-500% more than their equivalents.[7,20] This financial burden can add to hesitation or noncompliance to a strict observation of the GFD.

CONCLUSION

What we can learn from the included data is a GFD is only significantly beneficial to patients with diagnosed CD. Patients with diagnosed CD who experience migraine and switch to a GFD are likely to experience fewer and less severe migraines. Counseling regarding the potential of weight gain and financial burden should be discussed. Additionally, more research is needed to address the needs of those with NCGS and migraine that are unable to detect if a GFD is affective or if there is better approach with the utilization of nutritionist or gastroenterologists.

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