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Celiac Disease and Migraine Headaches: Current Knowledge and Future Directions

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SUMMARY

Background:

Migraine headaches and celiac disease are widespread problems affecting millions of patients worldwide. Celiac disease is an autoimmune disease in which the consumption of gluten leads to the development of an abnormal immune response in the intestines and the atrophy of intestinal villi. The most characteristic clinical symptoms of celiac disease are gastrointestinal symptoms. Nevertheless, manifestations of the nervous system, including migraines, are also sometimes noted. A gluten-free diet is the only effective therapeutic approach for patients with celiac disease. It reduces symptoms and halts the progression of the disease. Neurological symptoms, including migraines, are frequent extraintestinal manifestations. In this study we aim to elaborate on current knowledge concerning both coexisting of migraines and celiac disease as well as effect of gluten free diet on headaches in patients with celiac disease, gluten intolerance and healthy individuals

Results:

Headaches, especially migraines, are more common in patients suffering from celiac disease. Numerous studies indicate that a gluten-free diet may help in the treatment of headaches and is also an effective way to stop the progression of celiac disease.

Conclusion:

Migraine headaches are quite common in patients with celiac disease, and a gluten-free diet may help alleviate them. The findings suggest the need for increased awareness of the co-occurrence of these two conditions. A gluten-free diet is the only effective treatment for celiac disease and can stop progression of the disease. Further research is needed to determine potential benefits of such a diet in patients with gluten intolerance or healthy individuals.

KEYWORDS: Celiac Disease; Migraine Disorders; Diet, Gluten-Free

INTRODUCTION

Migraine, a neurovascular disorder affecting over a billion people worldwide, is a serious health and social problem due to its frequency, leaving a negative impact on both the patients and their families, as well as society as a whole¹.

Celiac disease, an autoimmune disorder causing gluten intolerance, is also a highly prevalent condition. Although the exact number of patients worldwide is unknown, it affects approximately 1% of the general population and remains a significant challenge for public health globally^{2,3}.

In this article, we aim to review the literature on the co-occurrence of both diseases and how the treatment of celiac disease and gluten-free diet impact the occurrence of migraine headaches.

PREVALENCE

Migraine is a fairly common disease with its prevalence peaking in those aged 35-39 years. The 1-year period prevalence of migraine is frequently reported, but it is important to recognize that a single migraine day per year is sufficient to define an active headache disorder. Standardized methodologies have been developed for use in population studies worldwide, and of these, the 1-year period prevalence is estimated at 15% globally, with the lowest number found in China (9%) and the highest in Southeast Asia (25-35%). In Europe, The Eurolight project reported a 1-year prevalence of 35% after sex adjustment in multiple countries. In contrast, US-based estimates have reported a 1-year prevalence of 12-13%, which remains stable over time¹.

The number of individuals with celiac disease is difficult to estimate, but meta-analyses suggest that its prevalence varies from 1.4% (based on serologic test) to 0.7% when considering biopsy results worldwide. The average age of diagnosis in the United States is 38 years². Both diseases are more common in women.

According to Dimitrova AK et al., migraine occurs significantly more frequently in individuals with celiac disease, up to 3.8 times more often than in the general population⁴. This suggests that the number of individuals experiencing both conditions is quite substantial, and the authors of these studies suggest increased awareness of inflammatory bowel disease and celiac disease in individuals presenting with migraine headaches.

PATHOGENESIS

Celiac disease is an autoimmune disorder in which the consumption of gluten leads to an abnormal immune response in the intestines and the destruction of intestinal villi, especially in individuals with genetic predisposition. The vast majority of patients with celiac disease have been shown to have the human leukocyte antigen (HLA) genes HLA-DQ2 or HLA-DQ8, which are considered to be one of the most important genetic factors contributing to the development of the disease. When gluten is consumed by individuals with celiac disease, it triggers an immune reaction in the intestinal epithelium and lamina propria. This reaction leads to the production of cytokines such as IFN- γ , IL-12, and TNF by T lymphocytes, as well as the formation of antibodies against tissue transglutaminase. The consequences of this immune reaction are tissue damage and inflammation^{5,6}.

As for the pathophysiology of migraine, it remains incompletely understood. However, it is known that during a migraine attack, intracranial vessels on the side of pain dilate, and there is inflammation of the meninges. Peptides such as substance P, neurokinin A, and calcitonin gene-related peptide (CGRP) are released during this process, with the latter appearing to play a significant role^{7,8}.

The co-occurrence of celiac disease and neurological disorders encourages the search for common features in their pathophysiology. In the case of migraine and celiac disease, it appears that elevated levels of IFN- γ and TNF- α , which can contribute to an increase in the amount of CGRP and central sensitization, may be relevant factors^{7,9}.

SIGNS AND WHEN TO PAY ATTENTION

Although usually the clinical picture of celiac disease primarily consists of symptoms related to the gastrointestinal tract, such as diarrhoea, bulky, foul-smelling, floating stools due to steatorrhea, and flatulence, literature confirms that neurological symptoms are quite often observed as well, such as dementia, amnesia, ataxia, chronic neuropathy, headaches, delayed motor development, neuromyelitis optica, and decreased muscle tone¹⁰.

Research conducted in this area suggests that even 24% of patients diagnosed with celiac disease report headaches as the dominant symptom¹¹. Therefore, it is important to consider situations that require further diagnostic testing in patients seeking medical help due to headache. Such direction of diagnosis may be indicated by the data obtained during the medical interview. According to medical knowledge, the precise pathophysiological mechanism leading to the development of celiac disease is not known, but it is assumed that it is a combination of genetic factors and environmental influences. The risk of inheriting celiac disease from first-degree relatives is 20%, and among significant environmental risk

factors, the time of introducing gluten into the diet, caesarean section delivery, lack of breastfeeding, and early gastrointestinal infections should be mentioned¹².

For patients with migraines and a family history of celiac disease, as well as any other symptoms of the disease, particularly those related to the gastrointestinal tract, tTG-IgA antibody testing (98% sensitivity; 95% specificity) should be considered as an initial diagnostic test. It is also important to measure the total number of IgA antibodies to rule out any production defects that could result in false results.

However, only the results of a biopsy of the small intestine and a typical histopathological picture of villous atrophy and a reduced villi/crypt ratio can provide certain confirmation of the disease. It should be remembered that an endoscopic examination should be performed in patients exposed to the antigen, so recommending a gluten-free diet without confirmation of the disease is not recommended¹¹.

GLUTEN-FREE DIET

Elimination diet with exclusion of gluten is the only recognized way to manage symptoms and stop the progression of celiac disease. In the context of headache in these patients, it has been confirmed that adherence to a gluten-free diet contributes to a 50% reduction in the frequency and intensity of migraines. Moreover, the benefits of gluten elimination in the diet with respect to headaches were significantly more frequently observed in patients with migraines than tension headaches¹¹. Other studies have shown that strict adherence to this diet reduces the frequency and intensity of headaches in 75% of patients and causes their disappearance in almost 30%^{13, 14}.

There is insufficient evidence for the effectiveness of a gluten-free diet as a therapeutic approach in patients without diagnosed celiac disease, although some studies have suggested the possibility of reducing pain symptoms¹⁵. It is worth noting that the harms of such a diet may outweigh the somewhat hypothetical benefits. It should be taken under consideration that gluten-free products contain less fiber, iron, vitamin D, B-group vitamins, zinc, and phosphorus than regular products. They are also more calorie-dense and have a higher glycaemic index¹⁰. Introducing such a diet requires patient awareness and dietary counselling, in addition to strict gluten avoidance.

It is also worth considering the problem of people who are gluten intolerant for reasons other than celiac disease, such as non-celiac gluten intolerance or wheat allergy. These conditions,

which differ in pathophysiology and dependence on IgE antibodies, do not require such strict gluten elimination and may also coexist with headaches. Unfortunately, there is insufficient evidence for the effectiveness of gluten avoidance in relieving headaches in this patient group¹⁰.

CONCLUSION

In conclusion, celiac disease and migraine headaches are both highly prevalent conditions that pose significant challenges for public health globally. Studies have shown that adherence to a gluten-free diet contributes to a reduction in the frequency and intensity of migraines, particularly in patients with diagnosed celiac disease. However, there is insufficient evidence for the effectiveness of a gluten-free diet in patients without celiac disease, and the harms of such a diet may outweigh the benefits. It is essential to consider the problem of people who are gluten intolerant for reasons other than celiac disease, as there is insufficient evidence for the effectiveness of gluten avoidance in relieving headaches in this patient group. Despite the incomplete understanding of the pathophysiology of migraine, there appears to be a link between celiac disease and migraine, with elevated levels of certain cytokines contributing to an increase in CGRP and central sensitization. Overall, these findings suggest the need for increased awareness of the co-occurrence of these two conditions and the importance of individualized dietary counselling for patients with celiac disease and migraine.

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