Does a gluten-free diet affect the course of Hashimoto's disease? - the review of the literature

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Abstract

Introduction and purpose

The fashion for following a gluten-free diet is causing more and more people to opt for it. It is indicated in the treatment of celiac disease. Due to the high prevalence of Hashimoto's disease in the population and the lack of causal treatment for the disease, many researchers have tested the validity of gluten elimination for those burdened with it. This work aimed to review the results achieved so far and assess whether this diet has a real impact on the course of Hashimoto's disease.

A brief description of the state of knowledge

A PubMed database was searched for studies describing the relationship between gluten consumption and the course of Hashimoto's disease. Some studies indicated a potential beneficial effect of the introduced diet on thyroid function. However, these were mostly survey-based studies of questionable research quality. More reliable studies that took into account antibody and TSH levels showed no significant improvement in thyroid function in response to the diet.

Conclusions

Based on the studies reviewed, there is no need for a gluten-free diet in patients with chronic autoimmune thyroid disease. It has not been proven that gluten can provoke the body to produce autoantibodies that cause the destruction of thyroid tissue. It is more important to maintain a balanced diet rich in zinc, selenium, iodine, vitamin D3, and iron, as they are essential in the process of hormone production by the thyroid gland.

Keywords: Hashimoto's thyroiditis; Autoimmune thyroid disorders; gluten-free diet; gluten; hypothyroidism

Introduction and purpose

Hashimoto's disease is one of the most common autoimmune disorders of the thyroid gland. It is characterized by thyroid-specific antibodies, i.e. anti-TPO-against thyroid peroxidase and anti-Tg-Ab-against thyroglobulin. By destroying thyroid tissue, they cause a decrease in the number of hormones produced by the gland. [1] The level of antibodies is related to the severity of the symptoms of hypothyroidism present. The exact cause of the disease has not been fully elucidated. It is known that a number of interrelationships between genetic conditions, environmental factors, and epigenetic influences play an important role. [2]

The incidence is higher in women, with an age range of 30-50 years. [3]

The lack of characteristic symptoms makes it difficult to make a proper diagnosis. The main complaints are systemic symptoms caused by damage to the thyroid gland, resulting in primary hypothyroidism. The most common symptoms that patients observe in themselves include swelling of the face and hands, constipation, feeling cold, and hoarseness. [4]

Other autoimmune diseases often co-occur, including alopecia, celiac disease, and type 1 insulin-dependent diabetes mellitus. Patients with type 1 diabetes who have levels of anti-TG and anti-TPO antibodies above normal values are 18 times more likely to develop hypothyroidism, compared to those without antibodies. [5] In addition, up to 70% of women with polycystic ovary syndrome experience Hashimoto's disease. [6]

Autoimmune polyglandular syndromes of APS can also co-occur with Hashimoto's disease. In their course, there is dysfunction of several endocrine glands. Their common feature is lymphocytic infiltration in the involved organs and the presence of antibodies in the blood. [1]
Proper thyroid function is also dependent on the proper composition of the intestinal microflora. Microorganisms affect the intestinal-liver circulation of iodine. In response to homologous viral or bacterial antigens, lymphocytes responsible for the formation of autoimmune thyroid diseases can be formed, and then the cross-reaction occurs. This is the so-called molecular mimicry mechanism. [7]

Due to the lack of treatment for the cause of the disease, the vast majority of patients require levothyroxine for the rest of their lives. Therefore, there is interest in other treatment options for this ailment. The popularity of a gluten-free diet in patients with this disease is constantly growing, and its properties are controversial. The desirability of using a gluten-free diet has been verified by a large number of scientists. The aim of the study is to review the literature in search of the relationship between the use of a gluten-free diet and the course of Hashimoto's disease.

Material and methods
A comprehensive literature search using the PubMed database. The search strategy included the following keywords and header terms: " Hashimoto's thyroiditis " OR "gluten" OR " gluten-free diet "OR " hypothyroidism " OR " Autoimmune thyroid disorders ". The search was limited to articles published in English and Polish. The studies included in this review were based on eligibility criteria. Inclusion criteria for this review were: English or Polish language, full-text articles, published since 2000, and free access. If the article did not have an abstract, the full text was downloaded and analyzed. The article was not used in this analysis if the full text could not be downloaded. First, studies were screened based on title and abstract, and then eligibility was checked.

Treatment
The mainstay of treatment for Hashimoto's disease is pharmacotherapy. It consists of taking levothyroxine in a dose that depends on the progression of the disease and body weight. [8] An adequate diet is also important. It is necessary to supply nutrients that are important in the process of hormone production by the thyroid gland. Particularly important is the proper supply of the body with elements such as antioxidants, which are vitamins A, C, E, omega-3 acids, and polyphenols, but also with selenium, zinc, iodine, magnesium, and potassium. [8]

STATE OF KNOWLEDGE
Gluten-free diet
A gluten-free diet involves abstaining from eating grains such as wheat, rye, barley, and oats. [9] It is important to limit even medications that may contain the aforementioned grains as fillers. The high content of grain products on our menus means that there is a greater possibility of gluten sensitivity without celiac disease and celiac disease. Europeans in particular are at increased risk due to the high gluten content in their diets. In dermatitis herpetiformis-Duhring's disease, a gluten-free diet is also recommended. [9] In these patients, the intestinal villi are partially atrophied. [4]

Celiac disease and Hashimoto's thyroiditis
Celiac disease co-occurs in 2-7.8% of patients with Hashimoto's disease. This is much more common than in the general population. The reasons for co-occurrence of both disorders simultaneously may have different causes. Both diseases have an autoimmune basis and genetic factors play an important role in the pathogenesis of their onset. [1]

One of the main antibodies implicated in celiac disease is tissue transglutaminase tTG2, which deaminates gliadin. It is also present in other tissues, including the thyroid gland, making cross-reactivity a possibility. Not insignificant in the frequent co-occurrence of both diseases is the low serum levels of vitamin D3 and selenium in celiac patients, which causes thyroid dysfunction. [1] The frequent co-occurrence of both diseases has directed many researchers to the possibility of introducing a gluten-free diet as a therapeutic option in patients with chronic lymphocytic thyroiditis. Accordingly, several studies have been conducted to analyze this relationship.

Relationship between gluten-free diet and Hashimoto's disease - review of studies
In 2000, A.Ventura performed a study which involved patients with celiac disease and Hashimoto's disease. Both groups were given a dietary elimination of gluten. Those on the gluten-free diet experienced a significant decrease in thyroid peroxidase antibodies. However, thyroid hormone levels did not change. [10]

A 2011 study by Metso noted no significant differences in TSH and fT4 between the gluten-eating group and the elimination diet group. It was noted that patients with celiac disease were at higher risk of developing Hashimoto's. Their diet did not reduce their risk of developing thyroid disease during the study, which lasted 12 months. [11]

A 2016 study by Krzysztof Kus was conducted on 156 people with Hashimoto's disease. The study was conducted through questionnaires. 78% of the subjects who did not take levothyroxine declared a significant improvement in their well-being after the introduction of the diet. Half of the subjects in this group also observed a decrease in TSH levels. TSH values decreased with both pharmacotherapy and diet alone - but in this case, the decrease was much smaller. Note, however, that this study was only in the form of a questionnaire - which makes the reliability of the results hard to verify. TSH levels were reported by patients and determined in different laboratories. Moreover, the possibility of co-morbid celiac disease was not investigated in the patients. [3]

In 2019 R. Krysiak conducted a study on 34 women with Hashimoto's disease, which lasted six months. All participants were in a euthyroid state. They were divided into those who followed a gluten-free diet and those who had no dietary restrictions. The study resulted in the following conclusions: the diet reduced the serum titers of TPOAb and TGAAb in women in the euthyroid state, which correlated with an increase in the SPINA-GT index, but did not affect the concentration of thyrotropin and free thyroid hormones. The likely reason for the beneficial effect of diet on thyroid autoimmunity seems to be the improvement in vitamin D status and selenium metabolism. Important limitations of the study, however, are the small number of participants, the lack of randomization, and the fact that all the women studied were euthyroid. [12]

The 2021 study, performed on 92 Caucasian women aged 18-55 with diagnosed Hashimoto's disease, lasted 12 months. As in the previous study, the subjects were divided into a control group, which consisted of women who had a normal diet and those who followed a gluten-free diet. All patients were given levothyroxine. A randomization program was used in this study, and in patients with antibodies to tTG, a gastroscopy was performed to rule out celiac disease. Patients on a gluten-free diet without the coexisting celiac disease had a decrease in TSH and an increase in fT4, which did not occur in patients on a normal diet. This result is likely due to improved intestinal absorption of levothyroxine. In contrast, antithyroid antibody levels did not improve. [1]

Due to the presence of randomization, the larger group of subjects, the longer duration of the study, and the verification that the patients do not have coexisting celiac disease, it can be concluded that the 2021 study appears to be the most authoritative.

On the basis of questionnaires, the results of his study were based on S.Konieczny in 2019. 209 people underwent the study (81 people had Hashimoto's disease and 118 had celiac disease). An elimination diet was introduced in both groups. The overall quality of life and accompanying symptoms were assessed. Hashimoto's sufferers were asked to complete ThyPROpl questionnaires. After analyzing the results, conclusions were drawn that the elimination diet significantly improved well-being and reduced disease symptoms. The main change was in the improvement of digestive problems. [4] An important issue that undermines the credibility of this study is the fact that in Hashimoto's patients, the presence of celiac disease was not ruled out as a coexistence. Also, basing the results on questionnaire data makes the study unreliable. The lack of measurements of thyroid hormones makes it impossible to realistically assess the work of the gland in response to the diet.

**Discussion**

In light of the presented results, it can be concluded that a gluten-free diet can benefit Hashimoto's patients. A correlation between antithyroid antibodies, antigliadin antibodies, and glutamine transaminase is evident. However, studies indicating a positive effect of diet on the course of the disease are mainly based on questionnaires, which makes them unreliable. It should be also remembered that any elimination diet carries the possibility of nutritional deficiencies. Long-term use of an ill-balanced diet can cause many adverse health effects. The most common of these are reduced levels of vit B, D3, calcium, and iron, but magnesium, copper, selenium, and zinc deficiencies can also occur. In addition, metabolic syndrome and cardiovascular disease can develop. [4] Particularly increased risk of the above-mentioned disorders occurs when the patient eliminates gluten from the diet on his own. As of this moment, there are no studies that clearly define the need to eliminate gluten from the diet in Hashimoto's patients.

**Conclusions**
At present, there are no studies that directly indicate that gluten should be eliminated from the diet of patients with Hashimoto's disease. Due to the small number of studies, with inconclusive results, it is not recommended to routinely discontinue gluten in all patients. It is possible that dietary modification alone, toward healthy eating habits and more frequent consumption of fiber, may have positive effects. It is also extremely important to have adequate levels of selenium, iodine, zinc, vitamin D3 and iron-building cofactors that are involved in the formation of thyroid hormones. This is also important for the absorption of levothyroxine in the gut. [1] However, it is important to keep in mind the frequent co-occurrence of celiac disease in these patients. It is in these patients that dietary modification is warranted, as well as in patients with gluten sensitivity. Decreased iodine absorption, as a result of unrecognized celiac disease, will result in the deterioration of thyroid function. This is why screening for this condition in Hashimoto's patients is so important. [13] Based on the results of the study, it has been also proven that avoiding the consumption of gluten does not affect the concentration of thyroid hormones. Therefore, it is not a solution to the main problem in patients burdened with Hashimoto's disease.

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