REVIEW ARTICLE

THE ROLE OF DIET IN MULTIPLE SCLEROSIS

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ABSTRACT

Multiple sclerosis (MS) is a disease of the central nervous system (CNS), characterized by chronic inflammation associated with autoimmune damage to myelin and axons leading to neurodegeneration. Although the etiology is not fully understood, some factors that increase the risk of disease have been identified. One of the key elements of multidisciplinary approach to the management of MS is a properly balanced diet, e.g. Swank diet. Its main assumption is to reduce the supply of animal fats in favor of fats of plant origin, which contain polyunsaturated fatty acids omega-3. One of the factors influencing the course of the disease is vitamin D deficiency. In 80-90% it is synthesized by exposure to the sun, while the other 10-20% may be supplied with ingested food. Although elevated plasma homocysteine levels have been demonstrated in MS patients, there is no need to modify the supply of B vitamins. Further studies are necessary to show the correlation between the supply of B vitamins and the course of the disease. Due to the antioxidant effect, it is recommended to include products that are sources of vitamin A, E and C, glutathione, coenzyme Q10. It is also beneficial to include compounds from the polyphenol group: quercetin, resveratrol and curcumin. Through proper nutrition model it is also possible to reduce side effects of applied medications, such as constipation, what improves patients' quality of life. Diet therapy is a key element supporting pharmacotherapy in patients with multiple sclerosis.

KEY WORDS: multiple sclerosis, nutrition, diet

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INTRODUCTION

Multiple sclerosis (MS) is a disease of the central nervous system (CNS), characterized by chronic inflammation associated with autoimmune damage to myelin and axons leading to neurodegeneration [1]. Relapsing remitting multiple sclerosis (RRMS) is the most common form of the disease, accounting for about 85% of all diagnoses. Most patients with RRMS are young women. Secondary progressive multiple sclerosis (SPMS) typically evolves from RRMS. It has been estimated that as many as 40-50% of patients diagnosed with RRMS will progress to a form of SPMS after 10 years. Clinical distinction between the two forms of multiple sclerosis described above is difficult. The primary progressive form (PPMS) accounts for only 10-20% of all cases. It is characterized by gradual development with short, transient stages of remission. In contrast, the progressive-relapsing form is the least frequently diagnosed form of multiple sclerosis. It occurs in only 6% of patients. It has a continuous character, distinguished by acute bouts of the disease [2]. The literature also distinguishes the qualification of MS due to clinical variants which is divided into benign and malignant forms. The first type concerns about 10-15% of all cases, and the prognosis is difficult to determine and requires observation for at least 15 years. The malignant form is relatively rare, but usually has a rapid course and results in progressive disability or even death. The etiology of the disease is unknown, but factors have been identified that increase the risk of developing MS [3]. These include genetic, exogenous and environmental factors. Studies have identified more than 50 alleles whose presence is associated with increased disease risk. Genes for T-cell receptors, genes located on chromosome 6, genes associated with the human leucocyte antigen (HLA) system, and the presence of endogenous retroviruses in the human genome have also been implicated among the causes of multiple sclerosis associated with genetic factors [4]. Additionally, if a family member is diagnosed with the disease, the probability of having the disease is increased. Exogenous factors modulating the development of MS include smoking and vitamin D deficiency associated with lack of sunlight exposure. Environmental factors of greatest importance in the development of MS include latitude and month of birth, hygiene (stress), viral infections such as Epstein-Barr virus infection, human herpesvirus 6 (HHV-6) infection, and non-specific bacterial infections, including the involvement of rickettsial microorganisms (e.g. Chlamydia pneumoniae). It is worth noting that both Epstein-Barr virus (EBV) infections, month of birth and latitude are associated with vitamin D deficiency because its production is related to exposure to sunlight, and additionally one of its functions is to produce cathelicidin, which is an inflammatory mediator. MS belongs to a group of autoimmune diseases associated with chronic inflammation of CNS. All inflammatory factors, such as diseases with fever, which impair the conduction in nerve fibers, as well as obesity and smoking (active and passive) cause abnormal immune response with increased proinflammatory process in the body [5]. The development of MS may also be

influenced by sex hormones, especially estrogen levels. It has been observed that the incidence of relapses is lower in pregnant women, which is likely to result from high estrogen levels. However, this reported factor requires further study. The most common age of onset of MS is between 20 and 40 years. One of the key factors influencing the course of the disease is lifestyle change, as well as the proper diet [6].

THE AIM

The aim of the study was to present the role of nutrition in patients with multiple sclerosis.

REVIEW

SWANK DIET IN MULTIPLE SCLEROSIS

Diet is one of the factors that play a key role in the treatment of MS. A model of nutrition that is beneficial to introduce is the Mediterranean diet (MD) [7]. It was first described by Ancel Keys based on observations in southern Italy and Greece. It is classified as a diet primarily low in saturated fatty acids while increasing the supply of vegetable oils. MD was developed in the 1960s, but has since undergone numerous modifications [8]. A variation of the Mediterranean diet used to reduce the chronic inflammatory process, modifying the course of multiple sclerosis, is the Swank diet. This dietary model was developed by Roy Swank in the 20th century on the basis of ongoing research aimed at introducing a low-fat diet in 144 patients diagnosed with MS. Fat supply was limited to a maximum of 50 g per day, with saturated fats primarily limited to 15 g per day, with particular emphasis on the intake of animal fat and dairy products [9,10]. Currently, the Swank diet is often used by medical specialists to support the pharmacological treatment of patients with MS. The main assumptions of this model of nutrition are to limit products that are a source of saturated fatty acids and processed foods, while increasing the supply of vegetable fats rich in omega-3 polyunsaturated fatty acids (especially olive oil, canola oil, walnuts, flaxseed). Dietary sources of protein include lean meat and fish, and seafood. Swank believed that the course of multiple sclerosis is determined by abnormalities of lipid metabolism, especially cholesterol and triglycerides [11]. In a study conducted by Zhornitsky et al., a correlation was shown between the degree of disability of MS patients and the levels of total cholesterol and triglycerides. Elevated levels of LDL fraction as well as total cholesterol, with special emphasis on apolipoprotein B have been shown to be associated with adverse MRI findings in patients with multiple sclerosis [12].

IMPORTANCE OF SELECTED NUTRIENTS IN MULTIPLE SCLEROSIS

VITAMIN D

Vitamin D belongs to a group of steroid compounds. It is commonly found in two forms: as ergocalciferol (vitamin D_2) and cholecalciferol (vitamin D_3). Due to its chemical structure, it exhibits similar effects to steroid hormones. Its discovery did not occur until 1919. In 1974 Goldberg suggested that insufficient vitamin D levels may be correlated with abnormal lipid composition and unstable myelin, which may increase the risk of multiple sclerosis in genetically predisposed individuals. The first clinical studies were conducted in 1986. Vitamin D supplementation was shown to reduce the relapse rate by 50% in patients diagnosed with MS [13]. Vitamin D synthesis in 80-90% occurs under the influence of ultraviolet radiation, through exposure to the sun. It exhibits pleiotropic effects in the body, of which the most important ones include:

- maintaining homeostasis of calcium-phosphate metabolism,
- regulation of the nervous system function through proven anti-inflammatory effects in myeloid cells,
- regulation of the cardiovascular system through participation in myocyte contractility,
- strengthening the immune system by reducing inflammation as it inhibits the production of pro-inflammatory cytokines such as interferon,
- enabling cell proliferation, providing for the proper functioning of the musculoskeletal system,
- regulation of the nervous system through neuroprotective effects [14, 15].

Vitamin D as a prohormone undergoes a two-step metabolism, in the liver and kidney, which results in the formation of calcitriol, which by binding to vitamin D receptors (VDR) enables its pleiotropic functions. The multidirectional effects of vitamin D are related to the presence of VDR receptors in many organs and tissues of the body [16]. VDR receptors are located throughout the cardiovascular system, particularly in myocytes and fibroblasts. Vitamin D deficiency has been shown to adversely affect myocardial contractility as well as vascular tone. Too low levels of 25(OH)D cause elevated levels of parathormone, resulting in left ventricular hypertrophy. In addition, vitamin D determines the proper functioning of the immune system, because it has a limiting effect on autoimmunity by inhibiting the production of proinflammatory cytokines. A study by Sandberg et al. involving 153 patients from the Department of Neurology at the University Hospital of Sweden showed that high levels of 25(OH)D are correlated with a lower risk of axonal damage and axonal degeneration in patients with MS [17]. Vitamin D belongs to the group of fat-soluble compounds. It is estimated that the coverage of its requirement from food is about 10-20%. It is present in small amounts in oily sea fish, fish liver and eggs. It can be added to some foods, especially milk and dairy products, but mainly its synthesis occurs under the influence of ultraviolet rays through sun exposure. The best indicator to assess vitamin D resources is the measurement of serum concentration, because its half-life is about 15 days [18]. Vitamin D determines the proper functioning of the nervous system and, in addition, has an impact on the motor performance of patients. There have been studies in which the relationship between serum

vitamin D levels and the result of a test assessing the degree of disability in patients - Expanded Disability Status Scale (EDSS) - was demonstrated. On the other hand, it is worth noting that with the introduction of a dose of 20 IU per day, no improvement in the physical performance of MS patients was observed. In the case of vitamin D deficiency, a specialist should always consult the patient in order to choose a possible dose of supplementation [19].

B VITAMINS

The relationship between the supply of B vitamins and the development and course of MS requires further study due to varied, unclear results and limited clinical trials. According to the literature, B vitamins are crucial in the course of the disease in patients with MS because of their functions. They influence normal nerve conduction and additionally affect serum homocysteine levels. Although demyelination could be both a result of cobalamin deficiency and a result of MS, it is possible to differentiate between those diseases based on clinical features. In a study conducted by Najafi et al., there was no correlation between vitamin B_{12} deficiency and the degree of disability and duration of disease [20]. Elevated plasma homocysteine levels have been observed in patients with MS, while this theory needs further investigation. According to recent literature, there is no need to limit animal products that are sources of vitamin B_{12} or supplementation in MS patients. However, due to the influence of B vitamins on nervous system function, care should be taken to ensure their proper dietary supply [21].

POLYUNSATURATED FATTY ACIDS (PUFA)

MS is an autoimmune disease of CNS. One of the most important components ensuring the proper functioning of the immune system are fats. As early as in the 20th century, studies have shown that the consumption of saturated fatty acids is directly related to the course of the disease and the incidence of relapses [22]. Roy Swank in the 20th century developed an applied nutrition model based on the principles of a low-fat diet, which is still used in patients with MS. It has been observed that in regions where animal fat intake is reduced in favor of vegetable fats, the risk of the disease is lower. Particular importance has been attributed to omega-3 polyunsaturated fatty acids because of their antioxidant and anti-inflammatory properties. The inclusion in the diet of products that are sources of PUFAs, as well as other antioxidants (carotenoids, polyphenols, lipoic acid, selenium), is recommended due to numerous studies that have shown that oxidative stress is one of the most important causes of chronic inflammation, which consequently leads to demyelination and axonal damage [23]. The sources of omega-3 are: olive oil, rapeseed oil, walnuts, flaxseed, corn oil, safflower oil, grape seed oil and oily marine fish. Particular antioxidant properties are attributed to olive oil. One study demonstrated a protective effect of two naturally occurring triterpenes: oleanolic acid and erythrodiol on experimental autoimmune encephalomyelitis (EAE), which is considered the best available model to study the pathogenesis of MS. Administration of triterpenes nullified the severity of the disease in EAE mice by preventing an increase in inflammatory cytokines. The prophylactic use of olive oil in MS patients is currently recommended. At present, the results of studies are inconsistent and require further follow-up [24]. A randomized study by Martinez-Lapiscina et al. evaluated the effect of following a Mediterranean diet, with a focus on extra virgin olive oil, compared to a control group following a low-fat diet. The observations lasted 6.5 years. It was shown that subjects following a Mediterranean diet supplemented with olive oil had higher scores in the Mini-Mental State Examination and Clock tests. The differences in scores were statistically significant, suggesting a protective effect of olive oil on the occurrence of cognitive impairment [25]. On the other hand, studies have also shown that consumption of excess saturated fatty acids from animal products increases the risk of developing MS because demyelination is more likely to occur due to a change in the composition of fatty acids that build the myelin sheath, and additionally negatively affects the body's immune response [26].

IRON AND ANTIOXIDANTS

Iron is one of the components essential for the proper functioning of the nervous system. Disturbances of iron homeostasis in the body result in an increased risk of neurodegenerative diseases, including multiple sclerosis. The cause is most often changes in the regulation of iron transport proteins due to chronic inflammation, and abnormal functioning of the blood-brain barrier, which can result in accumulation of this component in the brain. The consequence of this phenomenon is degeneration of glial cells and neurons. According to magnetic resonance imaging studies, in patients with MS, excess iron accumulates most often in the gray matter of the brain. It has been shown that patients often have elevated markers of oxidative stress compared to controls. Further research is needed to clarify the role of iron in the pathogenesis of MS [27]. Factors that influence the chelation of iron with free radicals have been identified. The key components include: vitamin E and glutathione, which show protective effects. Glutathione interacts with hydrogen peroxide, which is then decomposed removed so that binding to free iron ions is reduced, while vitamin E shows strong antioxidant activity. Other antioxidants with proven neuroprotective effects include vitamin A, vitamin C, and coenzyme Q10. There is an additional group of products with strong antioxidant activity, which are worth to be included in patients' diet therapy. They include: curcumin, resveratrol, green tea and lipoic acid [28].

CONSTIPATION

Constipation is a consequence of pharmacotherapy as well as a neurogenic colonic dysfunction common in patients with MS. It occurs in 39-73% of patients and spasmodi-

cally reduces quality of life. Factors that increase the risk of constipation are an inappropriate diet low in dietary fiber, insufficient hydration, and the use of antidepressants and cholinolytics [29]. Patient education should be the basic element of therapy. It is recommended to include food products that are the source of dietary fiber: wheat bran, raw vegetables, dried fruits, flaxseed, and whole-wheat bread. Caution should be exercised when using products such as caffeine or products containing sorbitol, which accelerate intestinal transit. In the treatment of constipation it is also necessary to systematize the time and volume of meals, as well as to take liquids regularly. In MS patients with normal body weight, a normocaloric diet is recommended [30].

DISCUSSION

Diet plays a key role in the course of the disease in patients with multiple sclerosis. The recommended dietary model is the Mediterranean diet. Its main goals are to increase the intake of vegetables and fruits, limit the intake of products that are sources of saturated fatty acids (red meat, eggs, lard, butter), and limit the intake of table salt. Protein sources are primarily fish and seafood, as well as poultry. It is recommended to increase the supply of fats of vegetable origin, such as olive oil and canola oil. Currently, the dietary model to be introduced in patients with multiple sclerosis is the Swank diet, which is a variation of the Mediterranean diet. Several nutrients have been singled out for attention in nutritional support for MS patients. These include vitamin D, B vitamins, polyunsaturated fatty acids, iron and antioxidants. One of the most common effects of pharmacotherapy is constipation, which is commonly prevalent in MS patients. It is recommended to increase the supply of dietary fiber sources, increase the supply of fluids. It is also necessary to systematize the timing of meals and their volume. Proper nutrition plays an important supporting role in the treatment of multiple sclerosis, but patient education should be a fundamental component of therapy.

CONCLUSIONS

Diet is a key element supporting pharmacotherapy in patients with multiple sclerosis. The recommended dietary model to be introduced in patients with multiple sclerosis is the Swank diet, which is a variation of the Mediterranean diet. Nutrients that play a key role in nutritional support for MS patients are vitamin D, B vitamins, polyunsaturated fatty acids, iron and antioxidants. The most common effect of pharmacotherapy is constipation, this is why it is necessary to increase the intake of dietary fiber and fluids, as well as regulate meal times and meal volume.

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