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DIETARY INTERVENTIONS FOR SUPPORTIVE MANAGEMENT OF RHEUMATOID ARTHRITIS, SJÖGREN'S SYNDROME, AND SYSTEMIC LUPUS ERYTHEMATOSUS: A LITERATURE REVIEW

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ABSTRACT

Rheumatological diseases, including rheumatoid arthritis (RA), Sjögren's syndrome (SS), and systemic lupus erythematosus (SLE), affect millions worldwide. Standard therapy includes pharmacological treatment, physiotherapy, and, if needed, surgery; however, clinical improvement is not always achieved. Consequently, additional strategies such as dietary interventions are being explored. Chronic inflammation plays a key role in these diseases. Diets rich in anti-inflammatory components, particularly the Mediterranean diet, may reduce disease severity, symptoms, and inflammatory markers in RA and SLE. Intermittent fasting, ketogenic, and plant-based diets may also be beneficial. A literature review of PubMed using the terms "rheumatoid arthritis AND diet," "Sjögren's syndrome AND diet," and "systemic lupus erythematosus AND diet," alongside current rheumatology treatment guidelines, identified 30 relevant articles. Although evidence remains limited, positive findings support further research. Well-designed, evidence-based diets could complement pharmacological therapy, enhancing treatment outcomes and patient quality of life.

KEYWORDS

Dietary Interventions, Rheumatoid Arthritis, Sjögren's Syndrome, Systemic Lupus Erythematosus

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1. Introduction

Rheumatological diseases affect a large number of patients worldwide and include conditions such as rheumatoid arthritis (RA), Sjögren's syndrome, and systemic lupus erythematosus (SLE). Rheumatoid arthritis (RA), the most common autoimmune disease affecting the joints, is managed primarly through pharmacological therapy, physiotherapy and, when indicated, surgical interventions [1]. In Sjögren's syndrome, treatment mainly focuses on alleviating the associated symptoms or, in more severe systemic forms of the disease, on the use of immunomodulatory or immunosuppressive therapy [2]. Systemic lupus erythematosus affects multiple organs and typically is also managed with immunosuppressive and immunomodulatory pharmacotherapy [3]. A common feature of these diseases is the absence of casual treatment. Despite advances in therapeutic methods, some patients still do not achieve satisfactory clinical improvement. Therefore, other treatment methods are being explored to improve the patient outcomes. In recent years, growing attention here has been given to the potential role of using diet in supportive treatment. Some nutritional models, such as the Mediterranean diet, are believed to have anti-inflammatory effects, which can potentially be used to alleviate the symptoms of rheumatological diseases driven by chronic inflammation.

2. Aim of the study, materials, and methods

The aim of this work is to review the available literature on the potential use of dietary interventions as supportive treatment for rheumatoid arthritis, Sjögren's syndrome and systemic lupus erythematosus. The work reviews articles available on PubMed database. The guidelines of rheumatological societies regarding treatment were also used. The search terms included "rheumatoid arthritis" AND "diet", "Sjögren's Syndrome" AND "diet", and "systemic lupus erythematosus" AND "diet". Following abstract screening, 30 articles addressing the role of dietary interventions in the supportive management of selected rheumatological diseases were included in the review.

3. Literature review

Rheumatoid arthritis

Rheumatoid arthritis (RA) is a disease characterized by chronic inflammation of the joints, hypertrophy of the synovial membrane, production of autoantibodies and destruction of cartilage and bone. The most characteristic symptoms include pain, stiffness and swelling of the affected joints - most often the hands and feet. RA is one of the most common autoimmune systemic diseases. The exact pathogenesis of the disease remains unknown. It is known that genetic, epigenetic, and environmental factors, as well as stress, obesity, female gender and smoking contribute to an increased risk of developing the disease. Pharmacological treatment is mainly used in the treatment of RA. In addition, non-pharmacological interventions such as appropriate exercises, rehabilitation and diet are recommended. The inflammation characteristic of the disease can lead to increased lipid oxidation and peroxidation. Activated T and B lymphocytes and macrophages are the main cells infiltrating the joints. These cells produce cytokines such as tumor necrosis factor TNF-α, interleukin-1 (IL-1), interleukin-6 (IL-6) and matrix metalloproteinases (MMPs). In addition, neutrophils and immune complexes in synovial fluid participate in cartilage destruction through the action of MMPs, the complement system and reactive oxygen species. The resulting reactive oxygen species can react with various molecules, including DNA or proteins, causing destruction of joint structures. Therefore, oxidative stress is believed to be crucial for the pathophysiology of the disease. Reports in the literature indicate that natural antioxidants may reduce oxidative stress, enhance endogenous antioxidant levels, and consequently alleviate the severity of rheumatoid arthritis symptoms [4] [5]. Possible side effects and limited efficacy of drugs have led to an increase in interest in new therapeutic approaches, such as dietary modification. The American College of Rheumatology guidelines recommend the Mediterranean diet over any formally defined diet, with evidence level ranging from low to moderate. The guidelines recommend that a diet other than the Mediterranean be followed with evidence level ranging from very low to moderate. This is due to the small number of scientific reports and the varying results obtained in individual studies. The fact that appropriately composed diets have anti-inflammatory potential leads to the creation of further studies on the use of such an approach in therapy [6]. Available scientific sources include studies examining the effect of dietary interventions on improving the clinical condition of patients with RA. The study by Johansson et al. demonstrated an inverse correlation between adherence to the Mediterranean diet and the risk of rheumatoid arthritis, though this effect was limited to men with the seropositive variant who maintained high adherence to the diet. However, this study has limitations, because the subjects themselves assessed their diet using a questionnaire assessing the diet 1 year before the diagnosis of RA. Nevertheless, the obtained results allow us to conclude that the applied nutritional models may have an impact on the development of the disease [7]. Rheumatoid arthritis is also associated with an increased prevalence of cardiovascular diseases in affected patients. It is believed that the chronic inflammation that accompanies RA is a risk factor for the development of cardiovascular disease. The Mediterranean diet is known for its anti-inflammatory properties, which is why Zhan et al. in their study examined the effect of following a Mediterranean diet on the risk of developing cardiovascular diseases. An important conclusion that was drawn in the study is that the coexistence of RA and low diet adherence may be associated with the risk of heart disease [8]. Fasting is another strategy that has been evaluated in the studies. Búr et al. in their study examined whether the negative effects of poor nutrition can be counteracted by eating meals at appropriate times. The study was conducted on mice with induced arthritis, which were divided into 3 separate groups receiving 3 different treatment regimens for 4 weeks - group 1 received standard food, group 2 was fed according to preference, and the third received high-fat food. The animals were allowed to eat food only during the 10-hour active phase. In the TFR group (time-fed) animals, reduced neutrophil infiltration was observed compared to the other groups. Moreover, after the induction of arthritis in TFR mice, the number of leukocytes in the synovial membrane was significantly lower than in the other groups. Leptin and interleukin-1 beta levels were also reduced. This study shows that, in addition to the composition of the diet, the timing of meals may also be important, and even short-term fasting may be helpful in a non-pharmacological approach to the treatment of RA [9]. In a study by Tavakoli et al., 44 overweight or obese postmenopausal women with rheumatoid arthritis and moderate to low disease activity (DAS28) participated in an eight-week randomized controlled trial. Participants were randomly assigned to two groups. The study group was subjected to an intermittent fasting regimen, allowing for calorie-free beverages during the 16-hour fast and unlimited food consumption for 8 hours, with the understanding that the diet was designed with a 300-kcal deficit. The control group was given a traditional diet with 3 meals and two snacks. Compared to the control group, the intervention group showed significant improvement in several markers of oxidative stress and inflammation – a decrease in serum malondialdehyde (MDA), a decrease in the neutrophil-to-lymphocyte ratio and an increase in catalase levels. In addition, a significant decrease in liver enzymes was observed in the IF group, indicating a possible hepatoprotective effect. MDA is a marker of lipid peroxidation and oxidative stress, and catalase is an antioxidant enzyme that plays a role in protecting cells

from damage. The neutrophil-to-lymphocyte ratio is considered a new marker of inflammation that has been associated with disease activity in RA. This study provides knowledge on the potential use of IF (intermittent fasting) in the adjunctive therapy of RA [10]. The subject of available studies is also the use of the ketogenic diet. This diet is attributed to the effect on inflammation associated with the synthesis of β-hydroxybutyrate. This substance has a direct anti-inflammatory effect on the NLRP 3 inflammasome, which is involved in inflammation induced by monocytes. The state of ketosis can be achieved by following a ketogenic diet or consuming ketone precursors such as medium-chain fatty acids (MCFA), caprylic acid or capric acid. Interestingly, exogenous ketosis induced by MCT is independent of insulin levels during fasting or low to moderate carbohydrate intake, which indicates the possibility of inducing ketosis without drastic changes in diet. In the study conducted by Heidt et al., the effect of MCT supplementation on the activity of RA was examined in patients using a normal eating pattern. The subjects were divided into two groups. The first group took 30g of MCT daily for 8 weeks and 30g of MCT (medium-chain triglycerides) plus 30g of fiber for the next 8 weeks. The control group took 30g of LCT (long-chain triglycerides) for the first 8 weeks and 30g of LCT and 30g of fiber for the next 8 weeks. A significant difference was shown in the form of a decrease in the SDAI score in the test group at the end of the study. Both groups saw an increase in BHB, but it was significantly higher in the test group. VAS decreased in both groups after 8 weeks, but only in the test group the decrease was maintained after 16 weeks of intervention. The results of this study indicate that MCT supplementation may also be helpful in non-pharmacological therapy of rheumatoid arthritis. However, further studies are needed, because the discussed study was conducted on a relatively small group of patients [11]. Another strategy under investigation is the use of a plant-based diet. Walrabenstein et al. in their study, they examined the effect of a multidisciplinary lifestyle change program in people with RA, which included, in addition to physical activity, stress management and education, the use of a plant-based diet based on wholesome foods. The intervention group showed a greater decrease in DAS28 after 16 weeks of the study compared to the initial value than the control group. All changes in DAS28 components, i.e. ESR, patients' global assessment and the number of swollen and tender joints, were more favorable in the test group, although the difference in the decrease in ESR was not statistically significant. The decrease in DAS 28 was reduced in both seropositive and seronegative patients compared to the control group. In addition, the loss of body weight and body fat and the decrease in waist circumference were significantly greater in the study group than in the control group [12]. The studies described above, despite evaluating different dietary approaches, share several common features. First, they were conducted on relatively small patient groups (excluding the animal study). Second, all interventions produced varying degrees of benefit. These findings highlight the need for further research in this area.

Sjögren's syndrome

Sjögren's syndrome is a systemic autoimmune disease, the most common symptoms of which are sicca syndrome, fatigue and musculoskeletal pain. In addition, other systemic symptoms may occur. Patients with this syndrome also have an increased risk of developing lymphoma. The treatment of the syndrome is symptomatic and should be carried out by an interdisciplinary team. The severity of symptoms may vary from sicca syndrome observed in over 95% of patients to the systemic form of the disease requiring immunomodulatory and immunosuppressive treatment [13]. There are few studies in the literature on the possible effect of diet on the severity of disease symptoms. In the available case series of a nutritional protocol based on raw, whole plant foods, all three patients with systemic lupus erythematosus and Sjögren's syndrome reported resolution or significant reduction in the severity of symptoms after one month of using the protocol. Based on these descriptions, a clear cause-effect relationship cannot be established, but it can be suspected that dietary interventions may be a helpful strategy in reducing disease symptoms as an adjunct to pharmacological treatment [14]. In recent years, there has been an increasing number of studies on the association of the microbiome with various diseases. Such a relationship has also been studied in the case of Sjögren's syndrome. At present, according to the available knowledge, it is still not established whether microbiome disorders are a potential cause of the development of the disease. Numerous studies have presented indirect evidence for changes in the oral, skin or intestinal microbiome. Molecular mimicry is also suspected to be involved in a possible mechanism of autoimmunity, as well as deregulation of the immune response against the normal microbiome. Currently, individual reports provide only preliminary and indirect evidence, underscoring the need for further research on this topic [15].

Systemic lupus erythematosus (SLE)

Systemic lupus erythematosus (SLE) is a disease characterized by the presence of autoantibodies against nuclear antigens, the deposition of immune complexes in various tissues and chronic inflammation. This disease is most often diagnosed in women of reproductive age. The main goals of lupus treatment include preventing disease exacerbations and organ damage, as well as improving the quality of life and survival of patients. The primary treatment of the disease is pharmacological; however, additional non-pharmacological interventions may provide clinical benefits, which is why they have become the focus of research. The previously mentioned Mediterranean diet may also be helpful in the treatment of SLE [16]. Available studies provide evidence for the effectiveness of a diet rich in unsaturated fatty acids by reducing disease activity and improving HDL cholesterol levels, as well as anti-inflammatory effects and an impact on cardiovascular health. Polyunsaturated omega-3 fatty acids may affect disease activity through anti-inflammatory effects, increase HDL levels and improve their functionality by increasing the activity of enzymes related to their metabolism. In addition, these acids can reduce inflammation by decreasing the expression of proinflammatory cytokines (TNF-α, IL-6) and inhibit the nf-κB pathway. The role of omega-6 acids is not entirely clear, as it has been shown that excessive consumption of them can have a pro-inflammatory effect. It seems that the ratio of omega-3 to omega-6 acids in the diet is important [17]. When considering dietary interventions as a supportive approach in disease management, highly restrictive diets are not always necessary. In a study by Knippenberg et al., patients reported benefits from a diet emphasizing whole plant-based foods while limiting processed items. Various dietary models were used by participants, with the greatest benefits observed among those following a vegetarian diet [18]. The benefits of eating more fruits and vegetables may be due to the increased intake of dietary fiber. The available literature includes a study on patients with SLE, which reported an association between high dietary fiber intake and reduced systemic inflammation [19]. The standard Western diet is characterized by a high consumption of so-called free sugar, which is considered a factor that increases inflammation in the body and promotes diseases such as obesity or metabolic syndrome. The role of this component in autoimmune diseases has not yet been fully understood. A study by Correa-Rodríguez et al. showed that the consumption of free sugars is higher in patients with active SLE compared to patients with the disease in clinical remission. Moreover, the first group was also characterized by a higher total consumption of carbohydrates and total sugars. The results of the study also indicate a statistically significant relationship between the consumption of free sugars and the activity of the disease, the presence of dyslipidemia and complications. In addition to the previously mentioned negative effects of sugar, it is believed that an excess of this component in the diet may promote the synthesis of free fatty acids in the liver and, consequently, the formation of metabolites of these acids and reactive oxygen species. In addition, this type of diet modulates the intestinal microbiota, which leads to the development of inflammation [20]. When considering dietary interventions in the management of rheumatological diseases, attention should also be given to supplementation. Numerous studies have examined the role of vitamin D deficiency, which is thought to potentially increase the incidence of autoimmune diseases. Clinical studies conducted on various populations of patients with lupus have shown an inverse correlation between serum vitamin D concentration and the disease activity index. SLE patients are also exposed to vitamin D deficiency due to the treatment used. This deficiency may result from the recommendation to avoid sun exposure or the use of drugs that have an adverse effect on vitamin D synthesis and metabolism [21]. Studies on the effect on reducing disease activity are not clear. The majority of studies reported either no change or only a minor reduction in disease activity. [22][23]. However, a normal level of vitamin D in serum in patients with lupus brings positive effects in the form of reduced osteopenia and osteoporosis, even when using corticosteroids [24]. In young patients with lupus, obesity or metabolic syndrome is often observed, which results in elevated levels of proinflammatory cytokines. Limited information is available in the literature regarding the exact pathogenesis of autoimmunity associated with a high-fat diet or obesity. A study was conducted to assess the effect of a high-fat diet (HFD) on the development of lupus. In the studied mice that were given this diet, a significant increase in body weight occurred compared to the control group. In addition, exacerbation of lupus symptoms was observed in these mice, with an increased frequency of skin lesions, proteinuria or splenomegaly and exacerbation of histological changes in the collected skin and kidney biopsies. Interestingly, the changes mentioned were more pronounced in females than in males [25]. Another study conducted on mice with SLE assessed the effect of a high-fat diet on the therapeutic efficacy of methylprednisolone. In the group treated with HFD and methylprednisolone, a smaller improvement in proteinuria was observed than in the group with a normal diet and methylprednisolone. Furthermore, HFD feeding was associated with elevated serum glucose levels during the glucose tolerance test. However, the high-fat diet had no effect on the change in antibody levels – regardless of the diet,

methylprednisolone treatment reduced the level of anti-dsDNA antibodies and lowered the level of IL-2, IL-10 and IP-10 in serum. Interestingly, after the drug was used, the reduction in the level of IL-6, MCP-2 and TNF-α occurred only in the group with a standard diet. The level of leptin, which increases the survival of autoreactive T cells and reduces the number of Treg cells, was significantly higher in the group with a high-fat diet. The results of this study suggest that a high-fat diet may affect the effectiveness of drugs used in SLE therapy, significantly reducing the therapeutic effect [26]. Regardless of dietary approach, attention should be given to the adverse impact of excess body weight on the severity of lupus symptoms. In the study by Meza-Meza MR et al. conducted on a group of 130 patients with SLE, it was shown that overweight patients had a higher disease activity score compared to the group without overweight [27]. Reducing calorie intake turned out to be beneficial in studies on mouse models - a reduction in disease symptoms and a reduction in the risk of atherosclerosis were observed by reducing inflammation, which is important due to the occurrence of increased cardiovascular risk in patients with systemic lupus erythematosus [28]. In other studies also conducted on mouse models, calorie restriction caused a reduction in the production of antibodies and the secretion of inflammatory mediators. The exact mechanisms of alleviating the symptoms of autoimmune diseases by limiting calorie intake are not fully understood. Leptin, which shows the characteristics of proinflammatory cytokine, is suspected of participating in the inflammatory reaction. In the study by Liu Y et al. fasting has been shown to be associated with reduced circulating leptin levels and increased Treg cell concentrations [29]. Furthermore, calorie restriction may delay the progression of kidney disease or prolong life in animal models of lupus [30]. As with rheumatoid arthritis and Sjögren's syndrome, evidence for the beneficial effects of dietary interventions on treatment outcomes in patients with SLE remains limited. Available studies have generally been conducted on relatively small cohorts, highlighting the need for research on larger populations to generate higher-quality evidence.

4. Conclusions

The role of dietary interventions in the supportive management of rheumatological diseases is undoubtedly worthy of attention. Currently, evidence regarding their benefits in the treatment of rheumatoid arthritis, Sjögren's syndrome, and systemic lupus erythematosus remains limited. The small number of studies, coupled with the small sample sizes, makes it difficult to draw definitive conclusions about the therapeutic value of different diets. Nevertheless, positive findings from some studies support further investigation. The development of well-designed diets with proven effectiveness in alleviating symptoms of these conditions could enhance pharmacological treatment outcomes and improve patients' quality of life.

Author's contribution

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