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The Role of Diet in Rheumatoid Arthritis Therapy – A Review of the Literature

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Abstract

Rheumatoid arthritis (RA) is an autoimmune chronic systemic connective tissue disease characterized by symmetrical arthritis, abarticular changes and systemic symptoms. The most characteristic symptoms are pain, stiffness and symmetrical swelling in the joints.

Including nutritional treatment in RA patients as a permanent component of therapy may have benefits in terms of weight regulation, reducing the risk of cardiovascular disease and osteoporosis, and an overall improvement in the patient's quality of life. Chemical compounds that exhibit anti-inflammatory effects include polyunsaturated fatty acids, polyphenols, and antioxidants. The use of herbal raw materials with anti-inflammatory properties is also becoming popular, but there is a need for further analysis to create official recommendations. Studies analysing the effect of consumption of anti-inflammatory bioactive substances on the disease activity have contributed to the search for a specific nutritional model optimal for patients with RA. Due to the high supply of anti-inflammatory substances and protective nature against the development of cardiovascular diseases, a balanced diet based on the principles of the Mediterranean diet is recommended. The aim of this review was to present the current knowledge on the role of diet in rheumatoid arthritis including the effect of bioactive substances supplementation on disease activity.

Key words: *rheumatoid arthritis, diet, antioxidants, polyphenols, polyunsaturated fatty acid*

Introduction

Interest in diet supporting the treatment of autoimmune diseases has increased over the past few years, which has contributed to the development of scientific research devoted to this topic. Rheumatoid arthritis (RA) is an autoimmune chronic systemic connective tissue disease characterized by symmetrical arthritis, abarticular changes and systemic symptoms. The most characteristic symptoms are pain, stiffness and symmetrical swelling in the joints of the hands and feet, but inflammation can also affect other joints. Patients with RA have an increased risk of developing diet-related diseases, including obesity [1, 2].

Physical disability and the pain associated with it, with inadequate caloric supply, may contribute to the growth of adipose tissue, which in turn may cause joint pain and deformity. In a prospective cohort study conducted on the basis of the Canadian Early Arthritis Cohort registry, it was shown that overweight and obese patients were less likely to achieve sustained remission (sREM) during the first three years of disease [3]. The authors of the meta-analysis conducted in 2016 drew a similar conclusion. Obese patients were 40% less likely to achieve remission of the disease than patients of normal weight. Most of the studies included in the analysis also showed higher values of disease activity scores, including DAS and DAS28, calculated on the basis of the examination of 44 or 28 swollen and painful joints, red blood cell sedimentation rate and C-reactive protein concentration. The assessment also takes into account the general health of the patient, determined by the visual analogue scale (VAS). Reduced mobility has also been observed in obese RA patients. However, there was no association between obesity and increased mortality. Nevertheless, the authors of the study emphasize the need for further analysis to assess the impact of obesity in the treatment of RA [4]. Also important, in the context of nutrition therapy in RA, is the increased risk of cardiovascular diseases in patients with RA, due to the ongoing generalized, chronic inflammatory process influencing the development of premature atherosclerotic lesions in the coronary, cerebral and peripheral vessels [5].

In the recommendations created by the European League Against Rheumatism (EULAR) involving the prevention and treatment of cardiovascular diseases in patients with RA, lifestyle modifications such as healthy diet, regular exercise and smoking cessation were also recommended with appropriate pharmacological treatment [6].

Adequate nutrition is also important in preventing osteoporosis. Patients with active RA are at increased risk of bone loss, bone fractures and increased bone resorption. Another important osteoporosis risk factor is a low body mass index (BMI). Therefore, for the prevention of fractures, in addition to introducing pharmacological methods, appropriate nutritional treatment based on the proper supply of energy, calcium and vitamin D is recommended in patients with RA [7].

Including education-based dietary intervention, reducing excess body weight, and introducing healthy eating habits into RA therapy can improve the patient's quality of life and reduce the risk of comorbidities.

Health promoting properties of Omega-3 fatty acids

Polyunsaturated fatty acids are one of the most researched groups of bioactive compounds in the treatment of RA. Polyene fatty acids (PUFAs) are present in both animal and plant-based foods, but the metabolism of these substances in the body differs from one another. Due to the location of the first double bond from the end of the carbon chain, they are divided into the following families: n-9, n-6 and n-3 [8]. The first clinical trials investigating the effect of a diet rich in PUFA were made in 1985 by Kramer et al. [9]. It was shown then that the number of painful joints was reduced and morning stiffness was shortened in RA patients from the intervention group who were on a diet rich in polyunsaturated fatty acids, low in saturated fatty acids and additionally supplementing eicosapentaenoic acid (EPA) at a dose of 1.8 g/day. The study lasted 12 weeks. In turn, a randomized, double-blind, controlled trial showed that daily omega-3 supplementation in RA patients has clinical benefits and may reduce the need for pain medication. The experiment included 60 patients with an active form of RA and randomly assigned either

to a placebo group or one supplemented with omega-3 acids in the form of 2 capsules containing 1.8 g of eicosapentaenoic acid (EPA) acid and 2.1 g of docasahexaenoic acid (DHA). The study lasted 12 weeks for which the standard pharmacological treatment of patients was continued. A significant reduction in the symptoms of the disease and the intake of painkillers was observed in the group supplemented with omega-3 acids. Among patients reducing the dose of painkillers, 32% discontinued the use of painkillers altogether. There were no statistically significant differences in body weight change in patients from the intervention group [10].

Research analysis on the effect of polyunsaturated fatty acid supplementation in RA patients was also the subject of a meta-analysis by Gioxari et al. [11]. The analysis included 20 randomized controlled trials of at least 3 months duration. It has been proven that oral omega-3 fatty acid supplementation significantly improves the values of disease activity markers including early morning stiffness (EMS), tender joint count (TJC), erythrocyte sedimentation rate (ESR) and pain scale. Among the inflammation markers, only the concentration of leukotriene B4 was significantly decreased. The positive effect of supplementation was also noticed on the lipid profile. A significant decrease in triglycerides levels has been demonstrated in patients in the intervention groups, which may be beneficial in reducing the risk of developing cardiovascular disease in patients with RA.

The analysis also includes the intake of products rich in omega-3 acids in patients with RA. In a cross-sectional study by Tadeschi et al. [12] the relationship between fish consumption and disease activity was investigated. The data of the ESCAPE-RA cohort were used for the study. Based on the analysis of the Food Frequency Questionnaire (FFQ) collected from the RA patients, it was observed that patients who consumed 2 or more portions of fish per week had a significantly lower DAS28-CRP index compared to those who did not eat fish at all or one portion per month.

The pro-health properties of omega-3 acids are believed to be in their anti-inflammatory action as precursors of lipid mediators of inflammation, modelling the inflammation. Moreover, many studies on animal models have shown a lower production of pro-inflammatory cytokines: TNF-α, IL-1β and

IL-6, and a decrease in leukocyte migration when EPA and DHA acids are supplemented [13, 14].

Polyphenols and antioxidants

Other tested bioactive substances in RA therapy are polyphenolic compounds and antioxidants, commonly found in foods of plant origin, including turmeric, cinnamon, green tea leaves, citrus and berry fruits. The health-promoting properties of polyphenols are related to their antioxidant activity by participating in the inhibition of the production of reactive oxygen species, as a result of which they limit the transformation of organic compounds related to oxidation [15, 16].

An example of a phenolic compound with such an effect is quercetin, whose supplementation was the subject of studies by Javadi et al. [17]. Fifty women who did not smoke and did not take other supplements were randomly assigned to the study group receiving a supplement of quercetin at a dose of 500 mg/day as a capsule or the control group receiving a placebo. Physical examinations and biochemical measurements to assess disease activity were performed both before and after the intervention. Daily quercetin supplementation (500 mg/day) was shown to have a positive effect on pain and morning stiffness, and decreased disease activity. Additionally, after the end of the study, there was a difference between the groups in the concentration of tumour necrosis factor ($p = 0.04$) and in the erythrocyte sedimentation rate, but it was not statistically significant.

Similar results were obtained by the authors of a randomized, double-blind study analysing the effects of a pomegranate extract supplement in people with RA. Patients from the placebo group took 2 capsules with cellulose daily, while those from the research group took 2 capsules containing 250 mg of pomegranate extract. Compared to the control group, the study group showed a significant reduction in the DAS28 index and the Health Assessment Questionnaire (HAQ) score. In the intervention group, a reduction in the number of swollen joints, the intensity of pain and the erythrocyte sedimentation index were also observed [18].

Beneficial therapeutic effects were also observed in the case of supplementation with micronutrients with antioxidant properties. In an Iranian study in 2014, a group of 39 women with RA took a daily supplement of 50 g of selenium, 8 mg of zinc, 400 g of vitamin A, 125 mg of vitamin C and 40 mg of vitamin E for 12 weeks. The aim of the experiment, apart from showing the effect of supplementation with antioxidant compounds on disease activity, was also to analyse the concentration of enzymes involved in the reduction of oxidative stress. The results of the conducted studies showed a decrease in the DAS28 index and C-reactive protein concentration in sick patients, while the change in the number of painful and swollen joints was not statistically significant. In turn, the concentration of antioxidant markers – glutathione peroxidase (GPX), superoxide dismutase (SOD) and catalase (CAT) – increased significantly after the intervention [19].

In recent years, there has also been an increase in interest in phytotherapy, that is the use of herbal preparations, as an element supporting the therapy of joint diseases. Many plant materials have been shown to have unique anti-inflammatory and immunostimulatory properties. Such plants species are, among others: field horsetail (*equisetum arvense*), Indian ginseng (*withania somnifera*) and ginger (*zingiber officinale*). In addition, their use can alleviate the feeling of side effects caused by pharmacotherapy, especially digestive side effects. However, attention should be paid to the need for further research in order to create official recommendations of herbal preparations as a therapy supplementing standard treatment due to many aspects of concern, such as: drug interactions, low bioavailability, insufficient standardization and legal regulations introducing the supplement to the market [20, 21].

Nutrition models in RA

The effectiveness of supplementation with bioactive compounds in clinical trials contributed to the search for specific nutritional models that could support the treatment of RA. Most attention is paid to the Mediterranean diet due to its high supply of polyunsaturated fatty acids, fruits, vegetables, whole grains and low consumption of red meat. Literature data also indicate

its high effectiveness in the prevention of cardiovascular diseases, metabolic disorders and neurodegenerative diseases [22, 23].

A systematic review of randomized clinical trials conducted in 2018 analysed the effects of the Mediterranean diet on the prevention and the treatment of rheumatoid arthritis. Two prospective studies and two clinical trials were included for the evaluation. There was insufficient evidence to support the thesis that the Mediterranean diet was effective in preventing RA, and there was limited evidence for pain reduction as measured by the visual analogue scale (VAS). One study reported a reduction in DAS28 after the intervention. The authors of the analysis recommend conducting further studies with a longer duration and greater diversity of the population covered by the intervention. Nevertheless, the implementation of nutritional recommendations based on the principles of the Mediterranean diet may bring secondary benefits in patients with RA, e.g. reduce the risk of cardiovascular diseases [24].

Similar conclusions were drawn during the ADIRA study analysing a diet based on products with anti-inflammatory properties. RA patients were divided into an intervention group and a control group whose diet was based on the dietary recommendations for the Swedish population. The intervention group received products to build a diet rich in omega-3 acids, dietary fibre, fruit, vegetables and probiotics (*Lactobacillus plantarum 299v*). The study lasted 4 months, then participants switched diets. It has been proven that an anti-inflammatory diet changes the lipid profile in RA patients towards a less atherogenic profile. The same study also analysed the effect of this nutritional model on disease activity, but no significant reduction was achieved [25, 26].

Another popular diet today is a vegan diet that excludes animal products. Current literature data suggest it has a beneficial effect in the treatment of RA through a high supply of dietary fibre and antioxidants, increasing the bacterial diversity in the intestinal microbiome, which may potentially reduce inflammation. In a study published in *Nutrients* in 2019, a favourable ratio of Th1 lymphocytes to Th17 lymphocytes and a reduction in bone erosion markers were observed in RA patients who were on a high-fibre diet for 28 days. Moreover, a properly balanced vegan diet may have a positive effect on the regulation of body weight and lipid metabolism [27, 28].

Conclusions

Diet is currently a widely discussed aspect in supporting the therapy of autoimmune diseases. Numerous studies show a positive effect of bioactive compounds in the treatment of rheumatoid arthritis. A properly balanced and varied diet including products with anti-inflammatory properties can bring many therapeutic benefits, especially in reducing disease complications and the risk of obesity and cardiovascular disease in patients with rheumatoid arthritis.

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