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Nutritional Strategies for Rheumatoid Arthritis: Exploring Pathways to Better Management

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ABSTRACT

Rheumatoid arthritis (RA) is an autoimmune illness that affects the entire body, with the involvement of the joints and gradual bone and cartilage loss. Environmental and genetic factors contribute to the susceptibility to RA. A growing body of research in recent years has indicated that nutrition plays a major impact in both the risk and course of disease. Notably, environmental factors like dust, pollution, infections, and smoking are identified as potential contributors to systemic autoimmunity preceding symptom onset. Amidst this complexity, the role of nutrition emerges as a significant area of interest, with studies indicating potential links between dietary habits and the onset of RA. The article thoroughly investigates the impact of dietary choices on inflammation, drawing attention to the dichotomy of foods with either pro-inflammatory or anti-inflammatory effects. The Western diet, characterized by its high intake of red meat, saturated fats, and refined carbohydrates, is implicated in elevating inflammation, insulin resistance, and obesity, potentially increasing the risk of RA. Further, the intricate relationship between nutrition and inflammatory diseases is explored, emphasizing the impact of specific nutrients on inflammatory processes. Omega-3 and omega-6 fatty acids, crucial for cellular membranes and inflammatory regulation, emerge as potential therapeutic supplements for RA management. Additionally, calorie restriction and antioxidants are identified as influential factors in mitigating inflammation and disease activity in RA patients. The manuscript also examines the effects of various dietary components such as flavonoids, gluten, fasting, vitamin D, and probiotics on RA. Overall, the manuscript presents a comprehensive overview of the intricate relationship between diet and RA, shedding light on the potential avenues for leveraging nutrition as a tool for managing and potentially mitigating the impact of this complex autoimmune condition.
Keywords: Inflammation, Rheumatoid Arthritis, Nutritional Therapy, Omega-3 fatty acids, Joint pains, Antioxidants

INTRODUCTION

A chronic inflammatory and autoimmune illness, rheumatoid arthritis (RA) is characterized by systemic symptoms in addition to joint involvement [1]. There is a significant range in the disease's estimated global prevalence across various populations, ranging from 1% to 2% [2]. During the development of RA, genetic and environmental variables interact. The HLA class II molecule-encoding locus is home to the most significant genetic risk locus linked to RA. Environmental variables can cause immunological tolerance to self-antigens, such as citrullinated and carbamylated proteins, to be broken in genetically susceptible individuals [3]. Many environmental variables, including dust, air pollution, food, infections, and cigarette smoking, can lead to the development of systemic autoimmunity

and the production of autoantibodies years before symptoms manifest [4]. Nutrition and diet have drawn a lot of attention as possible environmental factors affecting the onset and progression of the illness. The results are still unclear even though a number of studies have revealed links between dietary practices—mostly with relation to the consumption of fruit, vegetables, or meat—and the onset of the disease [5]. A growing body of research has examined the role that nutrition and food may play as preventative and management strategies for RA in recent years [6]. The decreased incidence of RA in Southern Europe as compared to Northern Europe and North America can likely be explained by the Mediterranean Diet (MD), genetics, and other lifestyle variables [7]. This review's objective is to examine how diet affects both the course of RA disease and its severity.

Diet as a Risk Factor in the Pathogenesis of Rheumatoid Arthritis

Based on the characteristics of particular foods, dietary practices may be both a protective and a risk factor for disease. Certain food choices can really have an anti-inflammatory effect (red meat, salt, high caloric intake, etc.) or an anti-inflammatory effect (oil, fatty fish, fruit, etc.) [8]. The prevalence distribution of RA shows that there are more RA patients in Western countries than in the East or emerging countries [9]. The Western diet has been associated with a higher risk of RA mainly because it causes inflammation to rise, insulin resistance to be induced, and obesity. It is characterized by a high consumption of refined carbohydrates, a low ratio of omega-3 to omega-6 fatty acids, a high intake of red meat, and saturated and trans fats [10].

Nutrition and Inflammatory Diseases

Inflammation is the primary cause of many chronic diseases, including RA, diabetes, cancer, cardiovascular disease, and Alzheimer's disease. C-reactive protein (CRP) is a better predictor of diabetes and hypertension than body mass index [11-15]. Food metabolism and inflammatory processes are intimately related, and nutrition has a key role in the development of chronic diseases such as diabetes and obesity. Certain foods have pro- or anti-inflammatory qualities depending on the inflammatory status that a nutrient modulates [16]. Many studies have been conducted on the effects of fats and carbohydrates on inflammation. The quality of carbohydrates is affected by excessive fiber consumption, which lowers the absorption of carbohydrates and, consequently, the levels of inflammatory mediators such as CRP, TNF-α, and interleukin-6 (IL-6). Whereas omega-3 polyunsaturated fatty acids, which are included in fish oils, have inverse relationships with TNF-α, IL-1, and CRP, trans-fatty acids have pro-inflammatory effects [17]. The Mediterranean diet (MD), which is mostly prevalent in Southern Europe and areas that cultivate olives, is high in vegetables, fruits, legumes, vegetables, fish, and extra-virgin olive oil. It is also moderately high in dairy products, eggs, chicken, red meat, red wine, and herbs and spices [18]. Galland's research indicates that foods contained in MD have direct anti-inflammatory effects. Using extra-virgin olive oil is linked to a decrease in thromboxane 2 (TXB2) and leukotriene B4 (LTB4), which is not the case when using non-virgin olive oil or maize oil. After 26 days of tomato juice ingestion, TNF-α production decreases. Consuming black tea can lower CRP levels, leukocyte and platelet aggregation and activation, and reduce inflammatory response in healthy males. This is primarily due to the flavonoid component in black tea. Consuming moderate amounts of red wine helps to raise overall antioxidant capacity and HDL while lowering oxidized LDL, fibrinogen, CRP, and low-/high-density lipoprotein (LDL/HDL) [19]. In addition to downregulating adhesion molecules and boosting antioxidant defenses, flavonoids have the ability to inhibit cyclooxygenase (COX-2) and inducible nitric oxide synthase (iNOS), two enzymes involved in the synthesis of inflammatory mediators [20].

One of the most powerful antioxidants, lycopene, is a carotenoid molecule found in tomatoes, which are a major component of MD. Tomatoes and tomato-derived products are rich sources of lycopene, which has been shown to have positive effects on inflammation and cardiovascular risk by lowering the expression of adhesion molecules and inflammatory factors (IL-6 and CRP) and increasing endothelial function [21]. Crucial nutrients included in potatoes include dietary fiber, potassium, and vitamin C. Additionally, a number of potato components help to improve lipid profiles, lower blood pressure, and reduce certain indicators of inflammation [22]. For RA patients, eating fruits, vegetables, and olive oil can lower their chance of developing inflammatory arthritis [23]. Vitamins C and E, which have strong antioxidant qualities, are abundant in fruits and vegetables [24–26].

Dietary and nutritional effects on disease activity in patients with diagnosed with RA

Patients with RA are becoming more interested in self-management techniques for symptom relief, such as bracing or splinting, using hot or cold packs, going to physical therapy, and relaxing. Nutrition is important for managing disease and may affect how well treatments work. Research indicates that dietary consumption of omega-3 and omega-6 fatty acids, in particular, may have potential mechanisms for use as supplementary therapy for RA [27].

Omega-3 and omega-6 fatty acids

Important for phospholipid membranes, omega-3 and omega-6 fatty acids also have the ability to control inflammatory mediators [28]. Lipid mediators called eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are involved in controlling and mitigating inflammatory reactions. Pro-inflammatory compounds such as arachidonic acid (AA) and omega-6 fatty acids derived from animal sources function as precursors to mediators of inflammation such as prostaglandins and leukotrienes. Essential fatty acids that cannot be produced are linoleic acid (LA, an omega-6 precursor) and alpha-linolenic acid (ALA, an omega-3 precursor). Plant oils, wholegrain bread, cereals, and animal fats are the primary dietary sources of LA, while green leafy vegetables, flaxseed, and rapeseed oils are the primary sources of ALA [29]. The ideal ratio of omega-6 to omega-3 is 1-4:1, but due to the abundance of LA in the Western diet relative to ALA, this ratio can rise to 10-20:1. It has been demonstrated through studies that the omega-3 fatty acids (EPA and DHA) can lower inflammation in human macrophages by inhibiting the formation of pro-inflammatory eicosanoids, neutrophil chemotaxis, and endothelium migration. Additionally, they downregulate adhesion molecules on vascular endothelial cells and block the NOD-like receptor NLRP3 inflammasome, which promotes inflammation resolution and increases macrophage activity [30].

Calorie Limitation

Interleukin-1 beta (IL-1B) production is stimulated in RA by an augmented activation of the NLRP3 inflammasome and an altered inflammatory response, both of which contribute to inflammatory symptoms [31]. A low-carb ketogenic diet or restricted calorie intake demonstrated an anti-inflammatory impact via reducing the generation of IL-1β mediated by the NLRP3 inflammasome [32]. In a murine model, the ketone body beta-hydroxybutyrate (BHB), which is formed during a state of hunger, inhibits the activation of the NLRP3 inflammasome in macrophages and downregulates the production of IL-1B by human monocytes [33]. Two investigations looked at the impact of calorie restriction on inflammation in people who were either obese or non-obese. The initial investigation revealed decreased manifestation of IL-1 B and the NLRP3 inflammasome in adipose tissue [34], while the second study found that the caloric restriction group had lesser serum levels of TNF alfa than a control [35].

Antioxidants

Antioxidant nutrients, which are present in a variety of foods, work as scavengers of free radicals, preventing the growth of tumor cells, preventing the absorption of cholesterol, reducing inflammation, and regulating redox processes. They have a special role in nitric oxide release, inflammation, and oxidative stress prevention and delay of atherosclerosis [36-38]. Oxidative stress, increased reactive oxygen species production, lipid peroxidation, DNA damage, and decreased activity of antioxidant protection systems are characteristics of rheumatoid arthritis [3, 4]. Jalili et al. [39] in their study to evaluate the effect of antioxidants in clinical outcomes in RA patients reported that daily antioxidant supplementation reduced oxidative stress and disease activity in 40 female patients with RA, but it had no effect on the number of sore and swollen joints. In contrast, vitamin A, C, zinc, and selenium supplements did not reduce the activity of RA disease in an earlier study [40]. Similarly, Sahebari et al. [41] reported no correlation of low serum amounts of zinc and selenium with disease activity in RA.

Flavonoids

Plants and fungi contain phenolic chemicals called flavonoids, which have anti-inflammatory, antibacterial, and antioxidant qualities [42, 43]. The main active ingredient in soybeans, genistein, has a number of health benefits, including chondro-protective, immunomodulatory, anti-inflammatory, and anti-angiogenesis qualities. Research conducted both in vitro and in vivo demonstrated that genistein effectively suppressed the expression of MMP-9 in fibroblast-like synoviocytes of RA as well as TNF-α, IL-1B, and EGF-induced proliferation [44].

Gluten

Wheat grains include a protein called gluten, which in celiac disease causes an immunological reaction and may be an antigen in RA. In RA patients, a gluten-free, vegan diet can lower levels of anti-gliadin and anti-beta-lactoglobulin antibodies as well as lower disease activity [45].

Fasting

A restricted consumption of calories with vegetable juice and vitamin and mineral supplements is what defines subtotal fasting. Abstaining from food may encourage a reverse of the normal immunological condition associated with RA, which is defined by the activation of CD4+ T cells and their development into Th1 and Th17 lineages, by decreasing the quantity and activation of CD4+ lymphocytes. Fasting for seven to ten days may provide a temporary immunosuppression that lowers T cell activation [46]. While it has been shown that fasting reduces pain and inflammation (ESR, CRP), these effects are only temporary and do not alter the course of the disease [47].

Vitamin D

The severity of the disease limits exposure to UV light and reduces the synthesis of vitamin D, and this is associated to the progression of RA disease and hypovitaminosis D status. Research indicates that there is a reverse correlation between disease severity and blood levels of vitamin D [48]. Vitamin D supplementation decreased disease flares, pain levels, and Disease Activity Score 28 (DAS-28) in RA patients, although the effects were not statistically significant, according to a meta-analysis of nine randomised control trials (RCTs) [49]. A related study found that higher disease activity and an increased risk of RA were associated with inadequate vitamin D intake [50].

Probiotics

The Food and Drug Administration (FDA) defines probiotics as live microorganisms that improve health and lessen oxidative stress in the body. The two most common probiotics found in pharmaceutical and commercial products are *Lactobacillus* and *Bifidobacterium* [51]. Probiotics may be an additional treatment for RA given the role the microbiome plays in the disease's development and the alterations it experiences in RA patients. The pro-inflammatory cytokine IL-6 levels were shown to be lower in a meta-analysis of nine investigations, but the disease activity score remained unchanged [52]. *Lactobacillus casei* 01 was reported to improve RA symptoms and IL-10, IL-12, and TNF-α levels in the control group in a clinical trial with sixty female RA patients [53]. In contrast, another study on the use of probiotics in patients with RA did not find that daily *Lactobacillus casei* 01 treatment improved serum lipid levels or oxidative state [54].

CONCLUSION

This thorough investigation highlights the complex connection between nutrition and the complex terrain of RA. The combination of dietary factors, environmental triggers, and genetic predispositions reveals a complex interaction that affects the development, course, and severity of disease. The information provided emphasizes how important diet is for RA, both as a risk factor and as a possible treatment option. Dietary choices play a crucial role in regulating inflammatory processes associated with RA, as demonstrated by the Western diet's pro-inflammatory components and the Mediterranean diet's anti-inflammatory components. Additionally, the book highlights the possible therapeutic benefits of several nutrients, including probiotics, antioxidants, flavonoids, and omega-3 fatty acids, in reducing inflammation and treating symptoms of RA. These discoveries open up new opportunities for augmenting current treatments and may lead to pathways for patient-specific individualized dietary interventions. The relationship between nutrition and RA is still complex, despite its promise. To further understand this relationship, longitudinal research, randomized controlled trials, and a greater comprehension of the mechanisms underlying dietary influences on RA etiology and development are necessary.

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