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The Therapeutic Role of Different Dietary Patterns in Inflammatory Bowel Disease

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Abstract: ***Inflammatory bowel disease (IBD), as an incurable immune disease, diet plays an important role in its treatment. Various components in the diet affect IBD. On the one hand, the Western diet pattern rich in fat, sugar and red meat is associated with an increased risk of IBD onset, possibly by changing the composition and function of the intestinal flora and promoting the generation of an intestinal inflammatory environment. On the other hand, beneficial dietary strategies help control IBD. Specific dietary patterns are considered to help maintain intestinal health and may reduce the frequency of IBD attacks. In addition, in IBD patients, nutritional support is also an important aspect. For example, ensuring sufficient protein intake during disease outbreaks helps repair intestinal mucosa. In short, diet plays an undeniable role in the onset, disease course development and management of IBD.***

Keywords: Inflammatory bowel disease, Ulcerative colitis, Crohn's disease, Diet**.**

1. Introduction

Inflammatory bowel disease (IBD) is an idiopathic inflammatory gastrointestinal disorder. Its occurrence and development are influenced by numerous etiological factors, including genetic susceptibility, immune factors, and the gut microbiota. IBD consists of two subtypes: Crohn's disease (CD) and ulcerative colitis (UC). In most cases, mesalazine is the first-line treatment drug. In some patients, aminosalicylate enemas are added to mesalazine. If the treatment is ineffective, corticosteroids, immunosuppressants, or surgery will be selected [1]. At the same time, during the treatment process, patients with IBD seek nutritional guidance in the hope of helping to improve their quality of life and relieve symptoms. However, regrettably, research to date has not laid a solid foundation for constructing strong evidence-based dietary recommendations [2]. In the past decade, the treatment goals for Crohn's disease and ulcerative colitis have shifted from simply controlling symptoms to deep remission, including clinical remission and mucosal healing, with the ultimate aim of preventing disease progression and the occurrence of disability [3]. Given the particularity of IBD, in addition to drug and surgical treatments, the introduction of appropriate dietary and nutritional habits is a crucial element in the treatment. However, in medical practice, this aspect is still underestimated and often overlooked. The introduction of the Western diet (high in fat and protein, low in fruits and vegetables) is considered an explanation for the increased incidence of IBD [4]. A meta-analysis study showed [5] that the consumption of fruits (odds ratio: 0.57) and vegetables (odds ratio: 0.71) was associated with a reduced likelihood of developing IBD. Another study determined through a Delphi randomization study and meta-analysis that modifiable risk factors (such as diet) are a promising approach to prevent the progression of IBD [6]. These studies indicate that diet plays an important role in shaping the composition of the gut microbiota [7]. Patients' curiosity about diet and the lack of accurate advice force them to seek information from the Internet and other non-medical sources. This study aims to review the published research on the impact of different dietary patterns on the course of IBD to date.

2. Low Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols Diet (Low-FODMAPs)

Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols (FODMAPs) encompass low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols. Relevant foods include barley, rye, pears, milk, onions, aloe vera, etc. The intake of FODMAPs can alter the composition of the gut microbiota, affect the interaction between bacteria and the gut, and subsequently change gut function and trigger a series of symptoms [8]. Such substances are minimally absorbed in the small intestine. The short-chain carbohydrates that are not digested or absorbed enter the colon and are rapidly fermented by microorganisms. When bacteria in the colon rapidly ferment these carbohydrates, gases such as hydrogen, carbon dioxide, and methane are produced. These gases can lead to gastrointestinal discomfort, and the symptoms caused include increased flatulence, abdominal distension, and diarrhea, which are extremely similar to the manifestations during the flare-up period of Inflammatory Bowel Disease (IBD). A prospective randomized study conducted by Pedersen et al. confirmed the positive effect of LFD in relieving gastrointestinal symptoms associated with Irritable Bowel Syndrome (IBS) [9]. In this study, 89 patients (in the remission period or with mild to moderate exacerbation of IBD) were randomly assigned to the FODMAP-restricted diet group or the standard diet group for 6 weeks. Finally, the results of 78 people recruited for this study were analyzed. It is worth noting that among those following the exclusion diet, as high as 81% of individuals achieved the effect of dietary change, while only 46% of individuals in the normal diet group showed a response. After the intervention period, compared with other groups, the population after LFD had a significant decrease in the index for assessing the occurrence of IBS symptoms. However, this situation only applied to patients in the remission period, not those with mild to moderate exacerbation of IBD. The main improvements were a reduction in the duration and severity of abdominal pain, a decrease in defecation frequency, and an improvement in

stool consistency. In addition, it has been reported that a low FODMAP diet has a greater improvement in the quality of life of IBD patients [9]. Another retrospective study of 49 IBD patients showed that approximately 40% of individuals indicated that a long-term low FODMAP diet was comprehensively effective. The main complaints reported to have improved were abdominal pain and abdominal distension [10]. These results suggest that a low FODMAP diet may be related to the relief of gastrointestinal discomfort in IBD patients, although it does not affect intestinal inflammation. A meta-analysis shows that LFD has a beneficial effect in relieving functional gastrointestinal symptoms (FGS) in IBD patients, but it has no significant benefits in improving stool consistency and mucosal inflammation [11]. LFD can reduce IBS, and for Ulcerative Colitis (UC) patients with IBS, LFD can better relieve symptoms. However, adhering to such a diet can lead to weight loss [12].

Therefore, if this diet is adhered to for a long time, appropriate nutritional advice is essential to prevent insufficient nutrient intake and unexpected weight loss.

3. Specific Carbohydrate Diet (SCD) and Anti-Inflammatory Diet (AID)

The SCD excludes complex carbohydrates, sugars, and most dairy products and processed foods that are considered malabsorbed and pro-inflammatory [13]. In the first half of the 20th century, Dr. Sidney Haas first used complex carbohydrates and disaccharides as part of the SCD diet to treat celiac disease in children [14]. This diet is based on the premise that polysaccharides and disaccharides have low absorption in the gastrointestinal tract, and their indigestible components can lead to dysbiosis, disruption of the intestinal barrier, and the development of inflammation, which are the causes of celiac disease and IBD.A large-scale survey study conducted by Suskind et al. [15] involving 417 adult and pediatric IBD patients (43% of whom were diagnosed with Ulcerative Colitis, UC) found that the SCD had a positive impact on the health status of the subjects. The researchers observed a decrease in the frequency and intensity of disease symptoms, especially an improvement in the occurrence of abdominal pain and diarrhea. Laboratory results improved for 47% of the respondents, 33% of the subjects achieved clinical remission after 2 months on the SCD diet, and 42% of the subjects achieved remission after 6 months and 12 months of the exclusion diet. In an anonymous survey of 417 pediatric and adult IBD patients treated with the SCD, 36% of the patients reported clinical remission within one to three months, and another 34% achieved remission after more than three months. Among the patients who achieved remission, 47% reported an improvement in abnormal laboratory test results [15]. Suskind et al. tested the effect of the SCD diet on IBD inflammation in another prospective case-control study [16]. This study included 12 children aged 10 to 17 years with mild to moderate IBD activity. All subjects included in the analysis were required to follow the SCD diet for 12 weeks. Laboratory tests were performed on the patients before the dietary change and at weeks 2, 4, 8, and 12. After 12 weeks, the researchers noted an improvement in the disease activity index of the recruited patients (in UC patients, the average Pediatric Ulcerative Colitis Activity Index, PUCAI value decreased from 28.3 to 6.7), a decrease in C-reactive protein (CRP) levels, and the normalization of serum albumin levels [16]. It is worth noting that there are few studies on the impact of the specific carbohydrate diet on IBD, and most of the existing studies are focused on children and Crohn's disease [17]. The decisive factors for the efficacy of the SCD may involve the main intestinal bacterial species, and thus may vary from patient to patient [18]. The SCD may have a positive impact on IBD; however, larger-scale prospective studies, especially those targeting adults, are needed to understand the effectiveness and safety of this diet. The AID is a revised version of the SCD. Its core lies in restricting pro-inflammatory carbohydrates, such as refined sugars, lactose, and most grain-derived carbohydrates, while introducing a large amount of anti-inflammatory products, namely prebiotics and probiotics. Probiotics can reduce the inflammation of Inflammatory Bowel Disease (IBD) in the following ways: beneficially altering the microbial community, inhibiting the proliferation of pathogenic intestinal bacteria, and improving and restoring the function of the epithelial and mucosal barriers. Studies have shown that under the AID model, changes in the microbial community are also associated with a reduction in inflammation [19].

In a study conducted by Altun et al. [19], it included a group of 40 Ulcerative Colitis (UC) patients treated with prebiotics (fructooligosaccharides) and probiotics (Lactobacillus plantarum, Streptococcus thermophilus, Bifidobacterium lactis, Lactobacillus acidophilus, Bifidobacterium longum). This study showed that the CRP levels of all subjects decreased, and clinical and endoscopic remission was achieved [19]. Another randomized trial analyzed the effect of Saccharomyces boulardii, Bifidobacterium breve, and Bifidobacterium bifidum on maintaining remission in UC patients, and the results showed that probiotics may have the same efficacy and safety as mesalamine alone [20]. However, since probiotic strains generally do not colonize in the colon, repeated and long-term administration is required, and long-term follow-up of the effect of this therapy is needed to obtain lasting benefits. A key issue with the SCD and AID is the risk of nutritional deficiencies, such as iron, calcium, B vitamins, and vitamin D. This is because some food categories rich in these nutrients are completely excluded. This is particularly important for children, as the above-mentioned nutritional deficiencies can delay their growth and development and lead to malnutrition. Given that the exclusion diet is highly restrictive, it should be used regularly and with caution.

4. Mediterranean Diet (MD)

The MD is characterized by a high intake of vegetables, fruits, grains, nuts, and legumes, which are rich in antioxidants and dietary fiber [21]; a moderate intake of fish and dairy products; an increased intake of unsaturated fats, while reducing the intake of saturated fats, meats, and sweets. Consuming fruits and vegetables are associated with a lower risk of IBD [22], possibly because they contain a large amount of water-soluble dietary fiber. The basic protective elements of the intestine are the mucosa and the microorganisms within it, and their condition and function depend on the intake of water-soluble dietary fiber [23]. Humans can produce approximately 17 types of enzymes for digesting fiber, while bacteria can

produce thousands of complementary enzymes that depolymerize dietary polysaccharides and ferment them into short-chain fatty acids that can be absorbed by the host, such as butyrate, propionate, and acetate. These substances have a positive impact on IBD, and dietary fiber provides a substrate for the bacteria in the distal intestine. At the same time, water-soluble dietary fiber does not stimulate the colonic mucosa and can promote the growth of microorganisms that produce butyric acid and propionic acid in the lumen of the large intestine. These substances have a protective activity on the intestinal mucosa, and butyric acid can also inhibit the synthesis of pro-inflammatory factors [24]. A comparative evaluation study conducted by Fernández-Bañares et al. investigated the efficacy of psyllium (10 grams, twice a day) and mesalamine (500 milligrams, three times a day) on the duration of remission maintenance over 12 months. The patients in this study were divided into three groups. The first group received psyllium seeds, the second group received mesalamine, and the third group received combination therapy (psyllium seeds and mesalamine). After 12 months of treatment, 30% of the patients in the combination therapy group experienced a worsening of UC, 40% in the psyllium seed group, and 35% in the mesalamine group. These results led the study authors to conclude that psyllium seeds and a diet rich in dietary fiber may have a similar potency to mesalamine treatment in maintaining UC remission [25]. For some patients with mild UC, a plant-based diet may relieve symptoms without the need for medications Numerous studies have shown that among IBD patients following the Mediterranean diet, the levels of CRP and fecal calprotectin are reduced, the quality of life is improved, and the proportion of probiotics increases [26-28]. The products consumed in the Mediterranean diet have a beneficial effect on the composition of the gut microbiota, and this nutritional plan may be one of the most effective dietary regimens for the therapeutic management of IBD patients [29]. The Mediterranean diet may be a suitable dietary choice for UC patients. However, it is necessary to make individual adjustments to this diet by selecting appropriate products and considering the technologies for the selected varieties and thermal processing techniques. A well-designed diet will provide appropriate energy, vitamins, minerals, and other bioactive compounds, and the intake of these compounds may be beneficial to the health of IBD patients.

5. The Impact of Some Foods on IBD

5.1 Red Meat and Processed Meat

Red meat is defined as all meat derived from livestock, including mutton, beef, pork, veal, goat meat, horse meat, etc. Processed meat is red or white meat made through methods such as smoking, salting (adding salt rich in nitrates and nitrites), curing, or adding preservatives. The study by Jowett et al. shows [30] that excessive consumption of meat, especially red meat and processed meat products, is highly likely to lead to the worsening of colonic mucosal inflammation in IBD patients. In the analysis, the average consumption of red meat and processed meat products among participants who experienced IBD exacerbation was as high as 172g/d, while that of participants without disease exacerbation was 124 g/d. Researchers believe that restricting the intake of red meat and introducing other protein sources in the diet may be able to prolong the duration of the remission period. Meat and processed meat also contain a large amount of organic sulfur and sulfate additives, which may increase the sulfate content of hydrogen sulfide produced by microorganisms, thereby causing damage to colonic mucosal cells. However, although other meats and fish also contain sulfur-containing amino acids, studies have found that they have no significant impact on the intestinal mucosa. In addition, the heme iron contained in red meat may promote the formation of N-nitro compounds in the intestinal lumen, leading to DNA adducts that cause mutations and have a carcinogenic effect. The nitrates and nitrites added to processed meat, as well as the compounds formed by red meat through curing, smoking (such as polycyclic aromatic hydrocarbons) or thermal processing (especially frying and grilling), can also promote the formation of N-nitro compounds in the body [31]. Therefore, IBD patients should reduce the intake of red meat and processed meat products. As a substitute, the intake of white meats such as eggs, milk, dairy products, and fish can be appropriately increased. Moderate addition of these foods has more benefits than adverse effects for IBD patients [32-33].

5.2 Herbs and Spices

Herbal products are widely used among IBD patients and have been proven effective in clinical treatment. Many dried herbs, such as thyme, oregano, and basil, are rich in polyphenols, which play a crucial role in the remission of IBD [34]. Among the spices, ginger and cumin also have certain anti-inflammatory effects, and turmeric deserves special attention in particular. Its main active ingredient, curcumin, has a wide range of anti-inflammatory, antioxidant, antifungal, and antibacterial activities. It can enhance apoptosis and also has anti-cancer properties [35]. The anti-inflammatory activity of curcumin, including its auxiliary role in the treatment of IBD, is based on the inhibition of effective myeloperoxidase function, the prevention of NF-κB kinase and IKB activation, and the reduction of interleukin-1 (IL-1) production and neutrophil infiltration [36]. Studies have shown that combining the drug treatment of IBD with curcumin supplements can improve the disease activity index, reduce the risk of recurrent exacerbation, and relieve disease symptoms. Most notably, it can improve mood and minimize the urgency of defecation [37-38]. Although curcumin supplements have achieved encouraging results in assisting the treatment of ulcerative colitis, researchers point out that more studies are needed to confirm the effectiveness and safety of higher doses. However, a small addition of curcumin can add diversity to the daily diet [38].

5.3 Nuts

Nuts are extremely nutritious foods, rich in unsaturated fatty acids, fiber, and protein. In addition, they also contain many vitamins and minerals (such as magnesium, potassium, copper, etc.) and other phytochemical components. Pistachios, pecans, and walnuts are abundant sources of phenolic compounds, including anthocyanins, flavonoids, proanthocyanidins, flavonols, isoflavones, flavanones, stilbenes, phenolic acids, and hydrolyzable tannins, etc. These components are all important antioxidants [40]. Pistachios have extremely high antioxidant and anti-inflammatory

potential, which may be due to their high content of γ-tocopherol, or the antioxidant effects of zinc and selenium. These two minerals are both considered to be closely related to the prevention of cardiovascular diseases and certain types of cancers [41]. In a prospective study [42], 32 healthy young men followed a Mediterranean diet for 4 weeks. In the following 4 weeks, pistachios were added to the Mediterranean diet, replacing approximately 20% of the monounsaturated fat content in the daily energy intake. The results showed that the pistachio diet significantly improved endothelium-dependent vasodilation, reduced the levels of serum interleukin-6, total oxidation state, lipid hydroperoxide, and malondialdehyde, and increased the content of superoxide dismutase, while the levels of C-reactive protein and tumor necrosis factor-α did not change significantly [42].

A randomized crossover trial of 18 healthy individuals showed [43] that compared with the end of the control period, consuming 42 grams of walnuts increased the relative abundances of Faecalibacterium, Clostridium, and Roseburia by 49% to 160%, while the relative abundances of Ruminococcus and Bifidobacterium decreased by 16% to 38%. In addition, consuming walnuts also reduced microbially derived pro-inflammatory secondary bile acids and low-density lipoprotein cholesterol [43]. Given that nuts are rich in oils and may cause diarrhea, they should be selected carefully and in moderation.

6. Conclusion

Although research on the relationship between diet and IBD has expanded significantly over the past decade, there are still many areas that remain unknown. Future research should aim to expand the scope of the clinical application of diet in IBD and delve deeper into the mechanisms by which diet exerts its effects. By evaluating specific immune cells, cytokines, and growth and nutritional mediators, we can gain a better understanding of how diet influences IBD. With further research and the integration of diet into clinical practice, dietary intervention is highly likely to become a major approach for managing IBD.

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