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Review Article

Food Avoidance in Patients with Ulcerative Colitis: A Review

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ABSTRACT

Inflammatory bowel disease (IBD) denotes to two principal groups of chronic relapsing inflammatory intestinal disorders including ulcerative colitis (UC) and Crohn's disease (CD). Medications are considered as the first-line of treatment in IBD management. Surgery as the second line of therapy is considered for patients who are intolerant to medications, but response rates continue to remain suboptimal and it is necessary to assess environmental factors such as diet that may not only help improve response to conventional therapy. Many patients with IBD reported that diet can affect the disease symptoms, employing avoidance diets while in remission. This review assessed food avoidance in patients with ulcerative colitis.

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Introduction

Inflammatory bowel disease (IBD) denotes to two principal groups of chronic relapsing inflammatory intestinal disorders including ulcerative colitis (UC) and Crohn's disease (CD) (1). IBD has an increasing trend, and changes in lifestyle can affect the prevalence of disease. The incidence of UC in Europe and North America was reported 8.3 to 10 per 100,000 people, and is higher than in Asia, Africa or South America. The disease has affected Caucasian patients more than non-whites, and has been more prevalent among females than males. The peak incidence was shown in patients between 20 and 40 years old, and the second peak among 60 and 80 years old population (2, 3). Prevalence and incidence of both UC and CD have increased in Asian and Eastern countries in the last decades due to extensive changes in lifestyle, particularly dietary habits (4, 5). Although the exact etiology of UC and CD is not fully understood, but there is a consensus that several causes including abnormal immune response, genetic and environmental factors are proposed to be involved in the initiation and progression of IBD (1, 6).

In UC, inflammation is usually limited to the mucosa, generally influencing the rectum and extending proximally, strictures being far less likely (7). The therapeutic aims in UC and CD are to induce and maintain remission also improvement in patient nutrition status and quality of life (8). Conventional medication in UC includes immune-suppression by targeting different pathways by administering immunomodulators and immunosuppressive medications to maintain remission, in addition to corticosteroids for controlling the active flares (9). Medications have been the first-line of treatment in UC management. And surgery as the second line of therapy in patients who are intolerant to the medications (10).

The major drugs used in IBD management are corticosteroids (e.g., hydrocortisone, prednisone, and prednisolone), 5-aminosalicylates (5-ASA) (e.g., sulphasalazine, and mesalamine), immunomodulators (e.g., azathioprine, 6-mercaptopurine, methotrexate and cyclosporine) and biologics (e.g., infliximab, adalimumab, and vedolizumab). Although several patients have responded to medications, but they can experience severe adverse side effects such as nephrotoxicity, fever, rash, drug hypersensitivity, hepatitis, pancreatitis, lymphadenopathy, abdominal pain, nausea, vomiting, diarrhea exacerbation, myalgia and an increased risk for lymphoma when using immunomodulators as some of the reported side effects. Surgery was also reported to be associated with resection of the severely damaged areas of the intestine or covering the complications such as strictures and fistulae (10). In recent years, due to dissatisfaction with these medications, great attention has been given to discover and to evaluate natural products that possess anti-inflammatory and antioxidant properties as complementary and alternative therapies.

Among medications, complementary medicine such as herbals have been widely used to control the symptoms and improve the quality of life (11-14), but response rates continued to remain suboptimal. So it is necessary to assess environmental factorssuch as diet that may affect response rate toconventional therapy (15, 16). Environmental factors were noted to affect and change the natural history of disease by altering both the host immune response and intestinal microbial composition (17, 18). Patients with IBD avoid a variety of foods. However, it remains unclear how this behavior varies across patients (19).

Patients suffering from UC are characterized by malnutrition from 20-70%, as the most important complication. About 71% of patients with UC have reported that diet can affect the disease symptoms, and employ avoidance diets (20, 21) and specificities in avoidance pattern revealed that the clinical response to dietary restrictions may differ according to the disease's characteristics (22). The dietary changes can be of concern if patients drastically reduce or completely eliminate nutritionally important foods/ food groups, as this may place them at increased risk for developing nutritional deficiencies, as well as a poor quality of life (23, 24).

Despite the lack of approved diet modification, IBD patients have also avoided several foods such as spicy ones, high-fiber foods, fruits, alcohol, dairy products, and vegetables. Many observational studies have described food avoidance in IBD in an attempt to identify dietary culprits related to digestive symptoms or relapse (25, 26). One of the exclusion criteria was shown to be specific carbohydrate diets. A case report of improvement of UC with specific carbohydrate diets was previously demonstrated in IBD (27). Specific carbohydrate diets compromise exclusion of all complex carbohydrates, grains, and refined sugars except the milk and honey confirmed in 10 patients, among whom 9 completed 12 weeks and 7 completed 52 weeks of specific carbohydrate diets (28) and 26 pediatric IBD patients on specific carbohydrate diets in conjunction with conventional therapy revealing improvement in IBD activity (29).

A case-control study significantly revealed a lower mean daily intake of monounsaturated fat, fiber, carbohydrates, calcium, and vitamins C, D, E, and K in comparison to controls, as a result of the exclusion of vegetables and fruit dairy and products (30). Western diets which are high in saturated fat, vitamins, refined carbohydrates, omega-6 fatty acids, low in fiber, and generally nutrient dense foods were shown to increase the risk of IBD (31). A semivegetarian diet allowing fish, milk and eggs once per week, and other meat once every 2 weeks (32), specific carbohydrate diets when removing most dairy products, all grains, and sweeteners except the honey (33), or anti-inflammatory diets such as modified fatty acid and carbohydrate ingestion, and increased prebiotic/probiotic intake can improve the clinical response (34).

The autoimmune protocol diet is an extension of the paleolithic diet and incorporates avoidance of gluten and refined sugar focusing on an initial elimination phase of food groups such as nuts and seeds, legumes, grains, dairy, eggs, coffee, nightshades, alcohol, refined/processed sugars, oils, and food additives (35). Clinical trials of fish-oil derivatives in IBD revealed mixed findings, showing beneficial effects, but did not show a clear protective effect in preventing clinical relapse. There are not enough data to suggest the use of n-6/n-3 polyunsaturated fatty acids in clinical practice (36).

In IBD, convincing evidence denoted to plant-based diets, with increased consumption of fruit/vegetables and less red meat intake to be suggested to patients with IBD in remission (37) denoting to the beneficial effect of fiber on disease outcomes in patients with UC (38). In mice with dextran sulfate sodium-induced intestinal inflammation, supplementation of polyphenols in dried apple peel powder caused normalization of inflammatory cytokines by regulating cellular signaling pathways and modifications in microbiota composition (39). Fiber has theoretically been shown to be beneficial effective to maintain disease remission through increased production of short-chain fatty acids playing an immunomodulatory role in intestine and favor the beneficial bacteria (40).

Also, food rich in dietary fiber have ingredients of aryl hydrocarbon ligands that may reduce intestinal inflammation (41). The role of germinated barley foodstuff (a water-insoluble dietary fiber) in UC showed a decrease in symptoms (abdominal pain and cramping) and C reactive protein (CRP) in germinated barley foodstuff (42). High vegetable intake was shown to be associated with a decreased risk of UC (43), but an increased consumption of sugar and soft drinks with low vegetable intake was demonstrated to be positively associated with UC risk (44).

In a study adding 60 grams/day of oat bran (equivalent to 20 grams oat fiber/day) to the diet of subjects with quiescent UC reported no signs or symptoms of colitis relapse after 12 weeks (45). Another study in patients with UC in remission comparing psyllium fiber versus mesalamine versus psyllium fiber plus mesalamine found continued remission at 12 months and slightly lower relapse rates in the mesalamine plus psyllium fiber group (46). Among 41 patients with UC in remission received 30 grams (three times daily) of germinatedbarley foodstuff in addition to conventional medication for two months, a statistically significant reduction in mean CRP was seen in the germinated barley foodstuff intervention group, as well as a significant reduction in abdominal pain and cramping (47).

In patients with IBD, the most popular diet in relief of symptom has been a gluten-free diet. In North America, 8% of patients were reported to actively consume a gluten-free diet to control the symptoms (48), while in UK, 28% of IBD patients reported to be gluten-sensitive, and 6% were gluten free (49). The protective effect of longchainn-3 polyunsaturated fatty acids (PUFAs) in UC was reported by inhibition of production of inflammatory cytokine and improvement in generation of anti-inflammatory eicosanoids (50, 51). A systematic review revealed an association with high total protein intake with the development of UC (52).

Active intestinal inflammation and poor oral intake during acute IBD are associated with myriad vitamin and micronutrient deficiencies of vitamin D, zinc, iron, and vitaminB12 (53). Even most of micronutrient deficiencies result from active disease and do not affect the disease pathogenesis, zinc and vitamin D in particular were shown to have key immunologic roles providing the hypothesis that repletion may also be of therapeutic effect. The association between vitamin deficiency and active IBD was seen in several studies (54). Vitamin D deficiency was noticed to be associated with increased risk of surgery, hospitalizations, and *C. difficile* infection in 3217 IBD patients (55).

Further normalization of vitamin D caused reduced odds of surgery in comparison to individuals who remained persistently deficient (55). The study of 70 UC patients in remission showed that a vitamin D level ≤35 ng/mL was associated with se in risk of relapse at 12 months (56). Vitamin D can have a modulating role on gut inflammation by increasing apoptosis of activated T helper type 1 cells and decreasing the release of pro-inflammatory mediators (TNF-alpha, interferon-gamma, ICAM-1 expression) in active IBD (57). Vitamin D through interaction with toll-like receptors and upregulation of cathelicidin antimicrobial peptide was demonstrated to enhance intracellular bacterial killing (58).

In 90 patients using high doses of vitamin D, it was demonstrated that a significant decrease in ESR and CRP happened (59). So vitamin D seems to have a prominent role in ameliorating gut inflammation. Zinc-sensing receptors were shown to have an important role in regulating colonic permeability and downstream inflammation through impact on occluding (60). Colitis animal models revealed an improvement in proinflammatory cytokines with zinc supplementation (61). Six months of zinc supplementation resulted into a significant decrease in several pro-inflammatory markers such as C reactive protein, interleukin-6, macrophage chemoattractant protein 1, and vascular cell adhesion molecule 1 (62). In follow up of 3,317,550 person-years, a high intake of daily zinc intake was shown to be inversely associated with risk of CD but not UC (63).

In 223 UC patients, an independent association of zinc deficiency was noted with subsequent surgery, hospitalizations, and disease related complications, with reduction in that risk in individuals who normalized zinc levels before the outcome (64). Home parenteral nutrition is used in patients in

whom effective enteral nutrition is not possible, or before operation to improve the patient's nutritional status (65, 66) and positively affect the IBD patient's general condition by increasing body mass index (BMI) and normalizing biochemical test findings indicating to the need to consider nutrition as an alternative to surgical intervention in severe IBD to reduce the complication rate (67).

Conclusion

The roles of diet and nutrition are major concerns of patients with IBD. There is scientific evidence from animal models and epidemiologic studies that dietary factors may influence both

the risk of developing and treatment IBD. However, the role of dietary interventions in the management of IBD still needs to be tested vigorously in patients. So, a better understanding of the role of various food components in intestinal homeostasis and the resident microbiota would be essential to unravel the environment interactions underlying IBD pathogenesis and offer dietary interventions with minimal side effects in relief of the disease symptoms. It seems that in management of UC patients, further well-designed prospective cohort studies studying various diet parameters with large sample size are necessary.

Conflict of Interest

None declared.

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