ADVANCES IN IBD

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Recent Research on Dietary Therapy for Patients With Crohn's Disease

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G&H What is the current understanding of the role of diet in the pathogenesis of Crohn's disease?

JL Diet is one of the potential environmental factors that contributes to the etiology of Crohn's disease. Some research has highlighted that consumption of a healthier diet, characterized by more fruits and vegetables and less meats, is associated with a lower risk of Crohn's disease. More recently, a number of studies have examined the role of ultra-processed foods and have fairly consistently shown an association between higher levels of consumption of ultra-processed foods and an increased risk of being newly diagnosed with Crohn's disease. An interesting aspect of this newer research is the possibility that the observations suggesting a beneficial effect of fruits and vegetables and a potentially harmful association of meats are actually surrogates for the potential harmful effects of ultra-processed foods.

G&H Why might diet have a role in Crohn's disease?

JL Why consumption of a more modern or Western diet would be associated with Crohn's disease is still up for debate. There are a number of different hypotheses. One of the hypotheses that has received a fair amount of attention over the past decade or so involves the potential impact of food additives on the gut microbiome and the mucus layer that protects the epithelium from luminal contents. Animal models have demonstrated that consumption of certain additives in the drinking water of mice that are predisposed to developing colitis was associated with thinning of the mucus layer, an effect thought to be mediated by changes in the microbiome. This thinning of the mucus layer allows for greater encroachment of the gut microbes on the epithelium and, therefore, greater interaction with the immune system. Although this is more difficult to study in humans, my colleagues and I conducted a study looking at one food additive, carboxymethyl cellulose, and were able to show that there were changes in the gut microbiome in people consuming the additive at high concentrations. We also found that some people may be predisposed to developing thinning of the mucus layer if they are particularly sensitive to that food additive.

G&H Could you discuss recent research examining the effects of a Mediterranean-style diet on Crohn's disease?

JL A number of studies have looked at a Mediterranean-style diet, but it is important to note that there is no singular Mediterranean diet; it can be thought of as consuming a diet that is characterized by more fruits and vegetables, olive oil as a predominant fat, and fish and lean meats (and, conversely, less consumption of red meats and processed sugars). From the standpoint of preventing the onset of inflammatory bowel disease, as mentioned earlier, it has been shown that people who followed a healthier or more Mediterranean-style diet were less likely to go on to develop Crohn's disease.

The use of a Mediterranean-style diet as Crohn's disease therapy has been studied in clinical trials, including the DINE-CD trial that my colleagues and I conducted. In that trial, we compared consumption of a Mediterranean-style diet to consumption of the Specific Carbohydrate Diet in patients with Crohn's disease who had mild to moderate symptoms. After 6 weeks of following these 2 different diets, we found very similar rates of symptomatic remission—approximately 45% in both treatment arms.

G&H Should the Specific Carbohydrate Diet also be recommended then for patients with Crohn's disease?

JL We designed the DINE-CD trial to compare the Specific Carbohydrate Diet with a Mediterranean-style diet because uncontrolled studies have suggested a benefit to the Specific Carbohydrate Diet. However, this diet is much more restrictive than a Mediterranean-style diet. When we designed the study, our theory was that if the Specific Carbohydrate Diet was not significantly better than the Mediterranean-style diet, it would make more sense to recommend the Mediterranean-style diet to patients. That recommendation would be based on several factors, one being that we were not able to demonstrate that the Specific Carbohydrate Diet was significantly better than the Mediterranean-style diet and the second being that a Mediterranean-style diet has been associated with numerous health benefits outside of its direct effects on patients with Crohn's disease. Therefore, in summary, the Specific Carbohydrate Diet has some evidence that it could be beneficial for patients with Crohn's disease, but the largest trial performed to date comparing this diet with a Mediterranean-style diet was not able to show that it was any better than the Mediterranean-style diet.

G&H Is there a role for a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols in patients with Crohn's disease?

JL It has been known for a long time that a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) is beneficial for patients with functional bowel disorders, including irritable bowel syndrome. Many patients with Crohn's disease also have irritable bowel syndrome. When medical and surgical therapies lead to complete control of inflammation, but patients continue to have symptoms, we often attribute these symptoms to concomitant irritable bowel syndrome. In these patients, treatment with a low-FODMAP diet can improve their general well-being and bowel symptoms, just as it does in patients who have irritable bowel syndrome without concomitant Crohn's disease.

G&H What research has been performed recently on the use of an Autoimmune Protocol Diet for patients with Crohn's disease?

JL There has been some research about the use of an Autoimmune Protocol Diet in patients with Crohn's disease, but most of the data come from uncontrolled studies. As a result, at this point in time, it is difficult to know whether an Autoimmune Protocol Diet would be better than any other healthy diet, such as a Mediterranean-style diet.

G&H Does supplementation of omega-3 fatty acids, fiber, or vitamin D have a role in the management of patients with Crohn's disease?

JL Two identical large clinical trials have looked at omega-3 fatty acid supplementation in the setting of Crohn's disease and have demonstrated that it was no better than placebo to improve Crohn's disease activity. As a result, I do not recommend omega-3 fatty acids to people solely for the purpose of managing their Crohn's disease. Of course, omega-3 fatty acid supplementation may be beneficial for other reasons, such as reducing triglyceride levels.

Fiber is thought to have a number of health benefits, but whether fiber supplements have a therapeutic benefit in patients with Crohn's disease is not well known.

Lastly, limited data suggest that vitamin D could have a potentially beneficial role in the management of Crohn's disease. On the other hand, patients who have Crohn's disease have an increased risk of osteopenia and osteoporosis, providing an alternate reason why it is useful to monitor vitamin D levels and supplement them when they are low. Patients with osteopenia commonly receive supplementation with calcium and vitamin D.

> When recommending that a patient follow one of the aforementioned restriction diets, it is important to figure out how the diet will fit in with the patient's cultural norms.

G&H What other defined diets or dietary modifications have been studied recently in patients with Crohn's disease?

JL In recent years, a fair amount of attention has been given to the Crohn's Disease Exclusion Diet, which is built around the concept of consuming several "mandatory" foods (including chicken breast, egg, potato, apple, and banana), limited amounts of other foods, and the exclusion of foods containing components thought to potentially be proinflammatory or to alter the gut microbiome (eg, foods containing gluten, carrageenan, and a number of other additives). This diet can be used with or without partial enteral nutrition (ie, the consumption of approximately 50% of one's calories from a nutritional formula). Several trials have suggested relatively high remission rates with the Crohn's Disease Exclusion Diet. In the most well-known trial, children with mild to moderate Crohn's disease that had been recently diagnosed were randomized to follow either the Crohn's Disease Exclusion Diet with partial enteral nutrition or exclusive enteral nutrition (ie, the consumption of 100% of one's calories from a formula). That dietary pattern continued for the first 6 weeks; subsequently, for the second 6 weeks, the percent of calories coming from formula went down to 25% in each group. The remaining 75% of calories were derived from the Crohn's Disease Exclusion Diet and the patient's usual diet in the 2 treatment arms, respectively.

At the end of 12 weeks, the Crohn's Disease Exclusion Diet arm had better outcomes using several different measures of clinical remission than the exclusive enteral nutrition arm, suggesting a therapeutic benefit of a dietary pattern consistent with the Crohn's Disease Exclusion Diet. However, this trial has raised questions regarding whether the benefits should be attributed to the diet or to the partial enteral nutrition.

Another trial that has been completed compared the Crohn's Disease Exclusion Diet with partial enteral nutrition to the same diet without partial enteral nutrition. This trial showed marginally better results when using partial enteral nutrition. When taking into consideration the first trial as well, the Crohn's Disease Exclusion Diet may have a therapeutic benefit even in the absence of partial enteral nutrition.

G&H What are the main challenges to using dietary-based therapy for Crohn's disease?

JL There are several challenges. It is very difficult for patients to sustain a changed diet. Diet is a very core component of our social existence, and there are many cultural aspects to diet as well. In some populations, there are also religious aspects to diet. When recommending that a patient follow one of the aforementioned restriction diets, it is important to figure out how the diet will fit in with the patient's cultural norms. It can be helpful to engage a dietitian to find ways to adapt whole-food diets.

In addition, almost all of these diets entail patients buying fresh ingredients and preparing their own meals, which is associated with both financial costs as well as time costs. For people with very busy lives, it can be difficult to figure out how they are going to fit this pattern into their lifestyle.

Last but not least, when gastroenterologists recommend a restriction diet, we are telling people to avoid certain foods and replace those calories with other foods, either ones that they already eat or new foods. There is a risk of perpetuating the belief that food is harmful and ultimately promoting food-avoidant behaviors. We have to be careful not to induce avoidant/restrictive food intake disorder by being highly proscriptive and restrictive in what foods we want people to eat.

> … patients can never go wrong by choosing a Mediterranean-style diet because it has many health benefits beyond Crohn's disease and may have the potential to improve symptoms of Crohn's disease as well.

G&H What dietary guidance has been provided recently by societies or official guidelines for patients with Crohn's disease?

JL The current dietary guidance varies. There are guidances from most societies at some level, but they are not entirely consistent. Some of the strongest recommendations involve the use of exclusive enteral nutrition in children as a first-line therapy for Crohn's disease. There is less consensus on whether this is appropriate for adults with Crohn's disease. Several professional organizations have also recommended the use of enteral nutrition prior to bowel resection for Crohn's disease, particularly for malnourished patients.

G&H What dietary recommendations do you typically give to your patients with Crohn's disease?

JL My approach is to try to understand the goal of each individual patient. Some patients want to use diet and nutrition as a primary therapy. Other patients want to use diet as an adjunct to their medical therapy. Still other patients want to use diet just to be healthier in general. I think the starting point is that patients can never go wrong by choosing a Mediterranean-style diet because it has many health benefits beyond Crohn's disease and may have the potential to improve symptoms of Crohn's disease as well.

It is important to separate out whether a patient is trying to use diet as their sole therapy or as an adjunctive therapy on top of medications. The dietary goal of many patients is just to improve their bowel symptoms while they rely on their medications to handle their inflammation. For some of these patients, this is where a low-FODMAP diet can be potentially useful. Other patients might try a Mediterranean-style diet or Crohn's Disease Exclusion Diet. For patients who want to try diet as their sole therapy, I usually start with a recommendation for the Crohn's Disease Exclusion Diet and strongly recommend that they meet with a dietitian to talk about how to implement it and make sure they are receiving adequate nutrition.

G&H What questions remain regarding diet and Crohn's disease?

JL The most fundamental question is, how does diet work in Crohn's disease? Even for exclusive enteral nutrition, which has been well studied, we have not figured out the mechanism by which it improves Crohn's disease. There are also other, more practical questions such as: What is the best way to use diet? What is the best dietary pattern to follow? How adherent does one need to be to these dietary patterns for them to be effective? How long does a patient with Crohn's disease need to stay on a diet? Does remaining on one of these diets long term change the natural history of the disease? These are all important questions that have not been adequately answered at this point.

Disclosures

Dr Lewis has consulted or served on an advisory board for AbbVie, Amgen, Arena Pharmaceuticals, Bridge Biotherapeutics, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Entasis Therapeutics, Galapagos, Gilead, Janssen Pharmaceuticals, Samsung Bioepis, Merck, Nestle Health Science, UCB, Pfizer, Protagonist Therapeutics, Sanofi, and Scipher Medicine. He has had research funding from Nestle Health Science, Takeda, Janssen Pharmaceuticals, and AbbVie. He has had educational grants from Takeda and Janssen Pharmaceuticals. He has performed legal work on behalf of generic manufacturers of ranitidine and 3M. He owns stock in Dark Canyon Labs.

Suggested Reading

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