JOURNAL OF MEDICINAL FOOD
J Med Food 22 (11) 2019, 1092–1099

DOI: 10.1089/jmf.2019.0063

REVIEW

Dietary Management of Pediatric Inflammatory Bowel Disease

Tanyaporn Kaenkumchorn[1] and Anil Kesavan[2]

[1]*Division of Pediatric Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Seattle Children's Hospital, University of Washington, Seattle, Washington, USA.*
[2]*Division of Pediatric Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Rush University Children's Hospital, Chicago, Illinois, USA.*

ABSTRACT Inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis, is a life-long relapsing and remitting condition characterized by inflammation of the intestine. While the exact pathogenesis of IBD is unclear, the current belief is that both genetic and environmental factors play a role in development of disease. Management options include nutritional, pharmacological, and surgical therapies. In particular, nutritional therapies for IBD have garnered significant interest due to their limited side effect profile, bowel-sparing nature, and naturalistic approach. This review will examine the role of diet in the pathogenesis and malnutrition in IBD, and will discuss dietary approaches to management of IBD, including exclusive enteral nutrition, specific carbohydrate diet, anti-inflammatory diet, and food supplements (specifically curcumin and long-chain *n*-3 polyunsaturated fatty acids). Past and recent literature on these subjects were reviewed in Medhub and Scopus databases for this review article with a focus on pediatric and high-quality publications. At this time, these approaches seem to be safe and show promise of an efficacious sole or supplemental role in the treatment of IBD, but randomized, prospective studies are lacking. Additional studies investigating these diets and food supplements are needed to provide more information on their efficacy, mechanism, applicability, and safety.

KEYWORDS: • ***anti-inflammatory diet*** • ***Crohn's disease exclusion diet*** • ***curcumin*** • ***exclusive enteral nutrition*** • ***selective carbohydrate diet***

INFLAMMATORY BOWEL DISEASE AND ROLE OF DIET IN PATHOGENESIS

The pathogenesis of inflammatory bowel disease (IBD) involves a complex interaction between genetic and environmental factors, which leads to an aberrant immune response to intestinal microbiota.[1] Close to 200 genetic loci have been linked to IBD, yet the exact manner in which these variants contribute to the pathogenesis of disease is not clear.[2] Environmental factors are also thought to play a role in the development of disease by altering the composition of gut microbiota, the mucosal immune system, and epithelial barrier function.[3] Diet plays a role in disease process in several ways. Certain foods are thought to increase proinflammatory cytokines, change intestinal permeability, and affect composition of the intestinal microbiota.[4] These changes may subsequently lead to chronic inflammation. A high-fat diet has been shown to alter the microbiome.[5] Nondigestible dietary carbohydrates, including inulin and fructo-oligosaccharides, have also been found to modify gut flora.[6] These effects are thought to have a role in the pathogenesis of IBD.

Diet and nutrition have been shown to be a modifiable risk factor in the development, treatment, and progression of IBD.[2,4,7] A diet high in fat, polyunsaturated fatty acids (PUFAs), omega-6 FAs, and meat has been connected with an increased incidence of IBD.[8] Studies have shown a correlation between increased intake of total fat, animal fat, and omega-6 PUFAs and incidence of Crohn's disease (CD) in particular.[9] Epidemiological studies have demonstrated a rising incidence of IBD in countries where this type of diet is more prevalent, such as Europe and North America, as well as in areas where IBD was previously uncommon.[10] This global increase has occurred with the spread of the ''Western'' diet throughout the world. It has been found that children of immigrants who move from countries with a low incidence of IBD have the same risk of developing the disease as local children when they move to a country with a high incidence of the disease.[2] This suggests that an environmental factor, such as diet, modifies risk of the disease. Conversely, diets high in fruits, vegetables, and fiber have been shown to be associated with a decreased risk of developing IBD.[11,12] Diet also has a substantial impact on patients' everyday life. In one recent study, 42%

Manuscript received 21 March 2019. Revision accepted 24 May 2019.

Address correspondence to: Anil Kesavan, MD, Division of Pediatric Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Rush University Children's Hospital, Professional Building, 1725 W. Harrison Street, Suite 710, Chicago, IL 60612, USA, E-mail: anil_a_kesavan@rush.edu

of individuals reported food affected their symptoms severely, while 51% of respondents indicated diet was important or extremely important in managing symptoms.[13]

The three principle models of dietary intervention are (1) supplementation with anti-inflammatory dietary components, (2) exclusion of proinflammatory dietary components, and (3) use of dietary formulas in place of a normal diet.[2] These approaches may be used exclusively or in combination. The goals of nutritional therapy in pediatric patients are to improve nutritional status, reduce disease activity, and correct pubertal growth retardation. This review will discuss in further detail an overview of malnutrition in IBD, followed by dietary approaches to management of IBD, including exclusive enteral nutrition (EEN), specific carbohydrate diet (SCD), anti-inflammatory diet, and food supplements (specifically curcumin and long-chain *n*-3 PUFAs).

NUTRITIONAL STATUS IN PEDIATRIC IBD

Pediatric IBD is associated with malnutrition, weight loss, bone mass deficits, and growth restriction.[14] There is general consensus in the literature that lean mass is reduced in children with IBD when compared to controls.[15] Lean mass deficits have been noted in up to 94% of children with CD and ~50% of children with ulcerative colitis (UC).[14] The clinical significance of protein-related deficiencies in pediatric IBD is not fully understood. Reduction in lean mass is likely due to a number of factors, including malnutrition, increase in circulating inflammatory cytokines, uses of glucocorticoid therapy, and failure to downregulate resting energy rate expenditure in a state of malnutrition.[14] In contrast to lean mass deficits, it is unclear if fat mass deficits occur in children with IBD, further studies are required.[15]

Nutritional deficiencies are common in IBD with up to 85% of individuals demonstrating evidence of deficiencies.[16] Nutritional complications are more common in patients with CD than UC, as well as in patients with active disease as opposed to remission. Up to 35% of newly diagnosed UC pediatric patients and up to 60% of newly diagnosed CD pediatric patients present with malnutrition.[17] On a molecular level, patients with IBD produce proinflammatory cytokines such as tumor necrosis factor alpha (TNF-α), interleukin (IL)-6, and IL-1β.[18] These factors, particularly TNF-α, lead to growth retardation through various mechanisms, including potential inhibition of growth plate chondrocyte maturation and as an independent mediator of growth hormone resistance.[19,20] Chronic nutritional deficiencies in IBD are likely due to inadequate caloric intake and anorexia.[21,22] Increased energy expenditure during relapse from chronic inflammation may contribute, although the evidence is conflicting. Identifying which vitamin and mineral deficiencies exist is paramount as chronic malnutrition is a treatable cause of growth failure in patients with IBD. This is particularly important since malnutrition is linked to poor outcomes in patients with IBD.[23]

IBD has been shown to lead to deficiencies of several micronutrients.[24] This occurs for a number of reasons that include insufficient intake, gastrointestinal mucosal loss, and as a side effect of pharmacotherapy.[24] Vitamin A and E deficiencies are reported in 16% of pediatric patients with IBD.[25] Other micronutrient deficiencies include zinc, niacin, copper, folate, vitamin D, calcium, iron, magnesium, and vitamin C.[26,27] Lower levels of vitamin B1, vitamin K, and selenium also are documented.[27] Vitamin B12 deficiency can result from ileal disease. These deficiencies are more likely in patients with CD, ileal inflammation, and resection.[28]

Nutritional complications of IBD include impairment of linear growth, weight loss, and delayed pubertal development. These findings are more common in children with CD than UC.[28] Additional nutritional concerns in pediatric patients with IBD include increased rates of osteopenia and osteoporosis, which also occur more frequently in children with CD compared to children with UC.[29] Anemia in IBD is common and occurs as a result of blood loss, chronic inflammation, hemolysis, myelosuppression, and micronutrient deficiency. Anemia is generally iron deficiency anemia or anemia of chronic disease.[28]

EXCLUSIVE ENTERAL NUTRITION

EEN typically involves a 6- to 8-week course of liquid formula, followed by the reintroduction of normal foods over 1–2 weeks.[30,31] Liquid nutritional formula is administered orally or through feeding tube. The three main types of formula vary by degree of protein hydrolysis. Formula may be elemental or polymeric. Polymeric formula mimics a general diet and consists of nonhydrolyzed proteins, carbohydrates, and fat.[32] At this time, there is no guideline on the ideal composition and administration of EEN.

The first reports on successful use of EEN in induction of remission in pediatric CD date back to the 1980s.[10] Since then, EEN has been thoroughly studied and has become a well-established nutritional approach shown to alleviate clinical symptoms, normalize laboratory abnormalities, improve nutritional status and linear growth recovery, and induce mucosal healing in pediatric CD.[10,30,33,34] EEN increases mucosal healing in patients with IBD, although the mechanism of action is not fully understood. It is thought that disease location can affect the efficacy of EEN. Isolated colonic disease does not respond to EEN as much as ileocolonic or ileal disease.[35]

In many centers across Europe, Japan, and Australia, the first-line treatment for induction of active pediatric CD is EEN.[30] In 2014, the European Crohn's and Colitis Organization (ECCO) issued revised consensus guidelines that recommend EEN as the first-line treatment for inducing remission in patients with luminal CD.[36] The advantages of EEN are induction of remission, control of inflammatory changes, mucosal healing, and improvement in growth.[30] Interestingly, treatment with EEN is more effective in achieving remission in children compared to adults.[37] Of note, although EEN suppresses inflammation in active CD, partial enteral nutrition does not.[38]

Historically, corticosteroids were the mainstay of therapy for inducing remission in pediatric patients with active

Table 1. Specific Carbohydrate Diet

	Allowed foods	*Foods to be avoided*	*Considerations*
Dairy	Homemade yogurt, dry curd cottage cheese, hard cheeses aged over 90 days (cheddar, swiss, Havarti, and colby)	Milk from animals, processed cheese (*i.e.*, American cheese), soft cheeses (mozzarella, ricotta, goat, feta, and cream cheese), margarine, kefir, and milk or cream-based products (ice cream, buttermilk, etc), no commercial yogurts	Can use plant-based milk (nut milks and coconut) as dairy substitute Homemade yogurt is fermented for a long time to reduce lactose content
Grains	No grains allowed	Wheat, rice, corn, quinoa, millet, amaranth, buckwheat, amaranth, teff, barley, spelt, rye, oats, triticale, and all grain products (pasta, cereal, bread, crackers, baked goods, and vegetarian meat substitute)	Can use nut flour (almond) and coconut flour
Vegetables	Nonstarchy, unprocessed vegetables (carrots, broccoli, mushrooms, onions, squash, tomatoes, spinach, peppers, cabbage, beets, artichoke, etc.)	Starchy vegetables (sweet potatoes, yams, parsnips, white potatoes, and rutabagas), canned or processed tomatoes, and packaged vegetables processed with additional sugar and additives	Organic preferred Fresh or frozen Some dried, canned, or pickled vegetables are allowed if they contain no sugars, additives, or preservatives
Fruit	Berries (blueberries, blackberries, cranberries, raspberries, strawberries, and boysenberries), stone fruits (plums, peaches, apricot, and nectarine), citrus (grapefruit, kumquat, lemon, lime, orange, and tangelo), banana, kiwi, pineapple, rhubarb, and dried fruit with no additives or sugar	Canned or dried fruit with additional sugar and additives	Organic preferred Fresh, unprocessed When initially adding fruit should be peeled and cooked Limit fruit if having diarrhea
Legumes	Dried navy beans, lima beans, black beans, cranberry beans, green (string) beans, lentils, split peas, and regular peas	Soy (in all forms), garbanzo beans, kidney beans, pinto beans, and canned beans of any kind	
Nuts and seeds	All nuts (almonds, walnuts, pecans, cashews, hazelnuts, macadamias, peanuts, etc.), coconuts	Flax seeds, chia seeds, hemp seeds, and nuts with a starch coating (most roasted nuts and commercially mixed nuts)	
Meat, poultry, fish, and eggs	Poultry (chicken, turkey, duck, goose, quail), fish, shellfish, lamb, beef, goat, venison, buffalo, rabbit, wild game, and all eggs allowed (preferably organic and free range)	Processed meats and fish (hot dogs, cold cuts, fast food, bacon, Spam, sausages, dried beef, and breaded products), smoked meats and fish	Organic preferred Either fresh or frozen is allowed Should be unprocessed, unbreaded, with no additional additives or sugar (including solutions) Some canned fish and cured meats may be safe if they contain no additives, preservatives or sugars (*i.e.*, canned tuna in water or its own juices)
Fats and oils	Vegetable oil, coconut oil, olive oil, sunflower oil, all nut oils, all seed oils (sesame, grapeseed, flaxseed, corn, and canola) pastured-cow or grass-fed butter, ghee, nut, and seed butters	Cooking oil with additives (cooking sprays), soybean oil, and vegan butter products	
Sweeteners	Honey	Agave, stevia, cane sugar, molasses, maple syrup, corn syrup, date sugar, coconut sugar, palm sugar, artificial sweeteners	No candy is allowed, except pure honey candy
Condiments, dressings, and vinegars	Most vinegars, homemade condiments and dressings	No commercial condiments or dressings, balsamic vinegar	
Binders, thickeners, and additives	Unflavored gelatin, baking soda (but not powder), and cellulose (in supplements only)	No preservatives of any kind, agar, carrageenan guar gum, potato flour, rice flour, sorghum flour, whey powder, fructo-oligosaccharides, seaweed or seaweed products, algae (like spirulina and chlorella), arrowroot, baker's yeast, baking powder, cellulose gum, cornstarch, cream of tartar, dextrose, hydrolyzed protein, mastic gum, natural flavors, pectin, Postum, sago starch, tapioca, and xanthan gum.	

Adapted from the NIMBAL website.

CD. However, steroids may decrease bone mineral density and compromise growth in an already vulnerable population. In a systematic review, EEN was shown to be as effective as corticosteroid therapy in inducing remission in patients with CD.[39] This meta-analysis of five randomized controlled trials of pediatric studies using EEN for CD in a total of 147 children demonstrated that EEN and steroids were of equal efficacy in the induction of remission in children with active CD.[39] Growth and development also improved in patients who received EEN.[39] Weight and body mass index have been shown to significantly improve after a first course of EEN, sustained at a 2-year follow-up.[30,40] Height was not significantly affected.[40] Further studies have shown not only clinical remission rates of EEN similar to steroid treatment but also had greater effect on mucosal healing and was associated with longer sustained remission.[41] There is evidence that children treated with EEN for induction have improved outcomes (reduced disease activity, improved linear growth, fewer relapses, decreased exposure to corticosteroids, and less requirements for immunosuppressive therapies) for up to 24 months when compared to children treated initially with corticosteroids.[42]

Clinical remission rates after a course of EEN vary from 60% to 88.5%.[30] A retrospective study in the Netherlands looked at 58 patients with newly diagnosed CD, with active disease, after a 6-week course of EEN and found a 71% complete remission rate ($n=41$), 26% ($n=15$) partial remission rate, and 3% ($n=2$) no response rate.[43] Nineteen patients discontinued EEN before treatment completion due to worsening symptoms or adherence issues.

Minimal side effects have been reported with EEN, including nausea, abdominal pain, flatulence, or diarrhea.[44] One of the main factors that limits success of EEN is patient adherence, particularly in pediatric patients. Nonadherence has been reported to range from 5% to 20% in various studies.[45]

SPECIFIC CARBOHYDRATE DIET

The SCD was first introduced by pediatrician Sidney Haas, MD, in the 1920s as a way to manage celiac disease and was published in textbook form in 1951.[46,47] In 1994, the diet became better known through Elaine Gottschall, whose daughter was treated by Dr. Haas for her UC with the SCD, in her book *Breaking the Vicious Cycle: Intestinal Health Through Diet*.[12,46] Today, the SCD is a diet used in patients not only with IBD but also with celiac disease, diverticulitis, cystic fibrosis, and chronic diarrhea. The diet claims to restore bacterial balance in the bowel, thus decreasing intestinal inflammation and purportedly inducing and maintaining remission in patients with IBD.[47]

The diet limits carbohydrates to monosaccharides (glucose, fructose, and galactose) found in fruits, nuts, honey, and fully fermented yogurt.[12] It excludes disaccharides (sucrose, maltose, isomaltose, and lactose) and most polysaccharides; all grains and starches, including wheat, barley, corn, rice, yams, and potatoes are excluded.[3] Vegetables containing more amylopectin (a branch-chained polysaccharide) than amylose (a linear-chain polysaccharide) are not allowed.[46] Food high in additives such as emulsifiers, preservatives, and processed meats are also excluded.[46] The SCD is a diet composed of protein (meat, poultry, fish, and lactose-free cheese), fruits, vegetables (except corn, yams, and potatoes), legumes (except chickpeas and soybeans), nuts, nut-derived flours, coconut flour, and honey[3] (Table 1). It is hypothesized that this diet decreases intestinal inflammation by changing the intestinal microbiome from a proinflammatory state to a noninflammatory state.[48] It is recommended that patients maintain the diet for 1 year during active disease, and for another year after symptom resolution.

There are currently limited studies formally evaluating the SCD and its effectiveness for the treatment of IBD. Patient perception seems to support use of the SCD, with 33% reporting remission 2 months after initiation of the SCD and 42% achieving clinical remission at 6 and 12 months (4% reported clinical remission before the SCD).[49] Suskind *et al.* retrospectively reviewed the medical records of 10 pediatric patients with CD who were treated with the SCD for a period of 5–30 months. Symptoms in all patients had resolved at a routine clinic visit 3 months after initiating the diet. Laboratory indices and fecal calprotectin either

Table 2. Inflammatory Bowel Disease—Anti-Inflammatory Diet

Prebiotics	*Probiotics*	*Balanced nutrition*	*Foods to avoid*
Steel-cut oats	Plain yogurt	Soluble fiber (fruits, vegetables, legumes, and nuts)	Refined sugar
Bananas	Aged cheese	Lean proteins	Milk and fresh cheese (except for aged cheese)
Ground flax seed, chia, and hemp seed	Fermented vegetables	Healthy fats (beans, nuts, olive oil, avocado, ground flaxseed, fish, and soy)	All grains (except for oats)
Garlic	Kefir		Trans fat (avoid partially hydrogenated oil)
Onions	Miso		Processed food
Chicory root	Pickles		Fast food
Artichokes	Raw honey		Corn
Leeks	Fermented cabbage		
Asparagus	Microalgae		

Adapted from the UMASS medical school website.

Table 3. Crohn's Disease Exclusion Diet

Foods to avoid
Gluten
Dairy products
Animal fat
Processed meats
Emulsifiers
Maltodextrin
Canned goods
Packaged foods

normalized or significantly improved at the follow-up clinic visits.[47] A prospective case series evaluated the effect of SCD in nine pediatric patients with CD and showed improvements in symptom scores at weeks 12 and 52. Capsule endoscopy findings, as measured by the Lewis score, improved at week 12, but not at week 52. Erythrocyte sedimentation rate and albumin otherwise remained unchanged throughout the study.[50] A small retrospective study of pediatric patients demonstrated persistent mucosal disease in patients on a modified SCD (rice, oats, quinoa, and potatoes added to diet), who were otherwise asymptomatic with normal or mildly abnormal labs (including calprotectin).[51] This raises concern for efficacy of this dietary intervention if mucosal healing is the therapeutic target.

Despite the positive clinical response seen on a strict SCD, the diet is difficult for many patients to maintain long term. Liberalization of the diet (by including foods such as rice, oatmeal, potatoes, corn, and cocoa powder) may be considered to increase patient adherence.[12] However, addition of new foods may lead to worsening disease activity. Baseline labs, including calprotectin, should be obtained 1 month after introduction of each new food item.[48] Patients with recurrence of symptoms or elevation of inflammatory markers should have the new food removed. Patients may experience weight loss on this diet and should be followed closely to identify development of any nutritional deficiencies.[48]

So, while the SCD shows promise in improving clinical symptoms in pediatric IBD patients, its efficacy in both serologic and histologic improvement of disease is unclear and further studies are needed.

ANTI-INFLAMMATORY DIET

One small retrospective case series has demonstrated potential efficacy of the anti-inflammatory diet (IBD-AID) in adults.[52] This diet has five components: (1) limiting certain carbohydrates (lactose and refined or processed complex carbohydrates), (2) ingestion of prebiotics and probiotics to help restore balance of intestinal flora, (3) decreasing total and saturated fats, eliminating hydrogenated oils, and encouraging intake of omega-3 FAs, (4) identifying missing nutrients and intolerances, and (5) modifying food texture to improve absorption of nutrients and minimize intact fiber[52] (Table 2). In this case series study, of the 11 patients who had complete data (age range 19–70 years), all patients were able to discontinue at least one of their prior IBD medications, and all patients showed reduction in IBD symptoms.[52] This study did not examine if any laboratory (improved inflammatory markers, etc.) or histologic improvement occurred with the diet. There is no current data to support the use of the IBD-AID in children. Future prospective studies are needed to determine the value of this diet in the pediatric population.

CD EXCLUSION DIET

The CD exclusion diet (CDED) involves elimination of processed foods, including gluten, dairy products, gluten-free baked goods and breads, processed or smoked meats, products containing emulsifiers, soy products, and canned or processed foods. The diet allows a limited amount of fiber (18–20 g of fiber) daily[53] (Table 3). A small prospective study of pediatric and adult patients demonstrates promise of the CDED in the treatment of patients with mild to moderate CD. Patients were placed on a dietary regimen of either partial enteral nutrition (50% of calories from formula) + CDED or solely CDED for a total of 6 weeks.[53] Within the pediatric subgroup, clinical remission was achieved in 24 of 34 patients (70.1%). Mean pediatric CD activity index decreased and normalization of inflammatory markers was also noted.[53]

FOOD SUPPLEMENTS

Efforts have been made to identify foods with anti-inflammatory properties and to study the effects of these

Table 4. Dietary Treatment Approaches for Pediatric Inflammatory Bowel Disease

	Exclusive enteral nutrition	*Specific carbohydrate diet*	*Inflammatory bowel disease-anti-inflammatory diet*	*Crohn's disease exclusion diet*
Induction therapy	Yes	No	No	No
Maintenance therapy	No	Yes	Yes	Yes
Clinical improvement	Yes	Yes	Yes (limited data)	Yes (limited data)
Mucosal healing	Yes	No	No (further studies needed)	No (further studies needed)
Limitations	Only utilized for induction therapy	Difficult to maintain long-term adherence due to restrictive nature of the diet	No current evidence supporting efficacy of this diet in the treatment of pediatric IBD	Limited evidence that demonstrates clinical and laboratory improvement with use of this diet. Further studies needed to validate efficacy of the diet in children

IBD, inflammatory bowel disease.

foods in the diet. While several food components have been studied to assess their role in the management of IBD, this review will focus on two prominent supplements in the literature: curcumin and long-chain *n*-3 PUFAs.

Curcumin, a plant derivative also known as the food spice, turmeric, is thought to have both anti-inflammatory effects and antioxidant effects.[54] The anti-inflammatory effects of curcumin may be due to suppression of the NF-kB signal pathway which affects IL-6, IL-1, and TNF-α.[55] In a tolerability study by Suskind *et al.*, 11 patients on IBD medication also took curcumin. There was a reduction in symptoms with the administration of 550 mg curcumin three times a day. No toxic effects were found.[56] Hanai *et al.* investigated the efficacy of curcumin on the prevention of UC relapse in a double-blind, randomized multicenter study. Eighty-nine patients between 13 and 65 years of age were randomized to receive a total of 2 g curcumin/day plus mesalamine or sulfasalazine (SZ), or placebo plus mesalamine or SZ, for 6 months. Relapse rates in the group receiving curcumin was 4.65% (2/43), compared to 20.51% (8/39) in the placebo group, $P = .040$. The curcumin group also showed improved Clinical Activity Index and Endoscopic Index scores ($P = .038$ and $P = .0001$, respectively), suggesting decreased morbidity.[57] Although curcumin appears to be safe and promising in improving symptoms and inflammatory indices, further studies are required.

Long-chain *n*-3 PUFAs have also been studied for their anti-inflammatory properties and potential beneficial effects. Fish-derived omega-3 supplements, including eicosapentanoic acid (EPA) and docosahexaenoic acid (DHA), have been reviewed in IBD. A pediatric study by Romano *et al.* assessed the use of long-chain omega-3 FA supplementation, in addition to amino-salicylic-acid (5-ASA) in pediatric patients with CD.[58] This study included 38 patients 5–16 years of age with CD in remission, who were randomized into two groups, either receiving 5-ASA and omega-3 FAs (including EPA and DHA) or receiving 5-ASA and olive oil placebo capsules for 12 months. Relapse rates were significantly lower in the group receiving omega-3 FAs, 61% (11/18), compared to placebo, 95% (19/20), $P < .001$.[58] Adult studies, however, have shown conflicting results.[59,60]

CONCLUSION

Treatment options for IBD are numerous and include pharmacologic agents, surgery, and dietary interventions. The side effect profile of these therapies varies greatly. Nutritional interventions may provide an avenue of intervention that is both safe and effective (Table 4). The aforementioned nutritional interventions including EEN, SCD, and nutritional supplements show promise in the treatment of pediatric IBD, although further studies are needed.

AUTHORS' CONTRIBUTIONS

All authors influenced the concept, wrote and revised the article, and approved the final version.

AUTHOR DISCLOSURE STATEMENT

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

1. Podolsky DK: Inflammatory bowel disease. *N Engl J Med* 2002; 347:417–429.
2. Lewis JD, Abreu MT: Diet as trigger or therapy for inflammatory bowel diseases. *Gastroenterology* 2017;152:398–414.
3. Lewis JD, Albenberg L, Lee D, Kratz M, Gottlieb K, Reinisch W: The importance and challenges of dietary intervention trials for inflammatory bowel disease. *Inflamm Bowel Dis* 2017;23: 181–191.
4. Huang EY, Devkota S, Moscoso D, Chang EB, Leone VA: The role of diet in triggering human inflammatory disorders in the modern age. *Microbes Infect* 2013;15:765–774.
5. Hildebrandt MA, Hoffmann C, Sherrill-Mix SA, *et al.*: High-fat diet determines the composition of the murine gut microbiome independently of obesity. *Gastroenterology* 2009;137:1716–1724.
6. Macfarlane S, Macfarlane GT, Cummings JH: Review article: Prebiotics in the gastrointestinal tract. *Aliment Pharmacol Ther* 2006;24:701–714.
7. Ananthakrishnan AN: Environmental risk factors for inflammatory bowel disease. *Gastroenterol Hepatol* 2013;9:367–374.
8. Hou JK, Abraham B, El-Serag H: Dietary intake and risk of developing inflammatory bowel disease: A systematic review of the literature. *Am J Gastroenterol* 2011;106:563–573.
9. Shoda R, Matsueda K, Yamato S, Umeda N: Epidemiologic analysis of Crohn disease in Japan: Increased dietary intake of n-6 polyunsaturated fatty acids and animal protein relates to the increased incidence of Crohn disease in Japan. *Am J Clin Nutr* 1996;63:741–745.
10. Penagini F, Dilillo D, Borsani B *et al.*: Nutrition in pediatric inflammatory bowel disease: From etiology to treatment. A systemic review. *Nutrients* 2016;8:334.
11. Ananthakrishnan AN, Khalili H, Konijeti GG, *et al.*: A prospective study of long-term intake of dietary fiber and risk of Crohn's disease and ulcerative colitis. *Gastroenterology* 2013; 145:970–977.
12. Burgis JC, Nguyen K, Park KT, *et al.*: Response to strict and liberalized specific carbohydrate diet in pediatric Crohn's disease. *World J Gastroenterol* 2016;22:2111–2117.
13. Kinsey L, Burden S: A survey of people with inflammatory bowel disease to investigate their views of food and nutritional issues. *Eur J Clin Nutr* 2016;70:852–854.
14. Thangarajah D, Hyde MJ, Konteti VK, *et al.*: Systematic review: Body composition in children with inflammatory bowel disease. *Aliment Pharmacol Ther* 2015;42:142–157.
15. Hill RJ: Update on nutritional status, body composition and growth in paediatric inflammatory bowel disease. *World J Gastroenterol* 2014;20:3191–3197.
16. Geerling BJ, Badart-Smook A, Stockbrügger RW, Brummer R-M: Comprehensive nutritional status in patients with long-standing Crohn disease currently in remission. *Am J Clin Nutr* 1998;67: 919–926.
17. Sawczenko A, Sandhu BK: Presenting features of inflammatory bowel disease in great Britain and Ireland. *Arch Dis Child* 2003; 88:995–1000.

18. Shamir R, Phillip M, Levine A: Growth retardation in pediatric Crohn's disease: Pathogenesis and interventions. *Inflamm Bowel Dis* 2007;13:620–628.
19. Ballinger A: Fundamental mechanisms of growth failure in inflammatory bowel disease. *Horm Res* 2002;58 Suppl 1:7–10.
20. De Pascalis B, Bianchi A, Satta MA, *et al.*: Growth hormone in inflammatory bowel disease. *Eur Rev Med Pharmacol Sci* 2006; 10:13–16.
21. Hartman C, Eliakim R, Shamir R: Nutritional status and nutritional therapy in inflammatory bowel diseases. *World J Gastroenterol* 2009;15:2570–2578.
22. Kirschner BS, Voinchet O, Rosenberg IH: Growth retardation in inflammatory bowel disease. *Gastroenterology* 1978;75:504–511.
23. Sandhu A, Mosli M, Yan B, *et al.*: Self-screening for malnutrition risk in outpatient inflammatory bowel disease patients using the malnutrition universal screening tool (MUST). *J Parenter Enter Nutr* 2014;40:507–510.
24. Kim YJ: Nutritional concerns in pediatric inflammatory bowel disease. *Korean J Pediatr* 2016;59:247–251.
25. Bousvaros A, Zurakowski D, Duggan C, *et al.*: Vitamins A and E serum levels in children and young adults with inflammatory bowel disease: Effect of disease activity. *J Pediatr Gastroenterol Nutr* 1998;26:129–135.
26. Filippi J, Al-Jaouni R, Wiroth JB, Hébuterne X, Schneider SM: Nutritional deficiencies in patients with Crohn's disease in remission. *Inflamm Bowel Dis* 2006;12:185–191.
27. Hwang C, Ross V, Mahadevan U: Micronutrient deficiencies in inflammatory bowel disease: From A to zinc. *Inflamm Bowel Dis* 2012;18:1961–1981.
28. Kappelman MD, Bousvaros A: Nutritional concerns in pediatric inflammatory bowel disease patients. *Mol Nutr Food Res* 2008; 52:867–874.
29. Sylvester FA, Wyzga N, Hyams JS, *et al.*: Natural history of bone metabolism and bone mineral density in children with inflammatory bowel disease. *Inflamm Bowel Dis* 2007;13:42–50.
30. Day AS, Whitten KE, Sidler M, Lemberg DA: Systematic review: Nutritional therapy in paediatric Crohn's disease. *Aliment Pharmacol Ther* 2008;27:293–307.
31. Escher JC, Taminiau JAJM, Nieuwenhuis EES, Büller HA, Grand RJ: Treatment of inflammatory bowel disease in childhood: Best available evidence. *Inflamm Bowel Dis* 2003;9:34–58.
32. Wedrychowicz A, Zajac A, Tomasik P: Advances in nutritional therapy in inflammatory bowel diseases: Review. *World J Gastroenterol* 2016;22:1045–1066.
33. Grover Z, Muir R, Lewindon P: Exclusive enteral nutrition induces early clinical, mucosal and transmural remission in paediatric Crohn's disease. *J Gastroenterol* 2014;49:638–645.
34. Day AS, Whitten KE, Lemberg DA, *et al.*: Exclusive enteral feeding as primary therapy for Crohn's disease in Australian children and adolescents: A feasible and effective approach. *J Gastroenterol Hepatol* 2006;21:1609–1614.
35. Afzal NA, Davies S, Paintin M, *et al.*: Colonic Crohn's disease in children does not respond well to treatment with enteral nutrition if the ileum is not involved. *Dig Dis Sci* 2005;50: 1471–1475.
36. Ruemmele FM, Veres G, Kolho KL, *et al.*: Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease. *J Crohns Colitis* 2014;8:1179–1207.
37. Verma S, Brown S, Kirkwood B, Giaffer MH: Polymeric versus elemental diet as primary treatment in active Crohn's disease: A randomized, double-blind trial. *Am J Gastroenterol* 2000;95: 735–739.
38. Johnson T, Macdonald S, Hill SM, Thomas A, Murphy MS: Treatment of active Crohn's disease in children using partial enteral nutrition with liquid formula: A randomised controlled trial. *Gut* 2006;55:356–361.
39. Heuschkel RB, Menache CC, Megerian JT, Baird AE: Enteral nutrition and corticosteroids in the treatment of acute Crohn's disease in children. *J Pediatr Gastroenterol Nutr* 2000;31:8–15.
40. Cameron FL, Gerasimidis K, Papangelou A, *et al.*: Clinical progress in the two years following a course of exclusive enteral nutrition in 109 paediatric patients with Crohn's disease. *Aliment Pharmacol Ther* 2013;37:622–629.
41. Berni Canani R, Terrin G, Borrelli O, *et al.*: Short- and long-term therapeutic efficacy of nutritional therapy and corticosteroids in paediatric Crohn's disease. *Dig Liver Dis* 2006;38:381–387.
42. Lambert B, Lemberg DA, Leach ST, *et al.*: Longer-term outcomes of nutritional management of Crohn's disease in children. *Dig Dis Sci* 2012;57:2171–2177.
43. de Bie C, Kindermann A, Escher J: Use of exclusive enteral nutrition in paediatric Crohn's disease in the netherlands. *J Crohns Colitis* 2013;7:263–270.
44. Borrelli O, Cordischi L, Cirulli M, *et al.*: Polymeric diet alone versus corticosteroids in the treatment of active pediatric Crohn's disease: A randomized controlled open-label trial. *Clin Gastroenterol Hepatol* 2006;4:744–753.
45. Rodrigues AF, Johnson T, Davies P, Murphy MS: Does polymeric formula improve adherence to liquid diet therapy in children with active Crohn's disease? *Arch Dis Child* 2007;92: 767–770.
46. Kakodkar S, Farooqui AJ, Mikolaitis SL, *et al.*: The specific carbohydrate diet for inflammatory bowel disease: A case series. *J Acad Nutr Diet* 2015;115:1226–1232.
47. Suskind DL, Wahbeh G, Gregory N, Vendettuoli H, Christie D: Nutritional therapy in pediatric Crohn disease: The specific carbohydrate diet. *J Pediatr Gastroenterol Nutr* 2014;58:87–91.
48. Obih C, Wahbeh G, Lee D, *et al.*: Specific carbohydrate diet for pediatric inflammatory bowel disease in clinical practice within an academic IBD center. *Nutrition* 2016;32:418–425.
49. Suskind DL, Wahbeh G, Cohen SA, *et al.*: Patients perceive clinical benefit with the specific carbohydrate diet for inflammatory bowel disease. *Dig Dis Sci* 2016;61:3255–3260.
50. Cohen SA, Gold BD, Oliva S, *et al.*: Clinical and mucosal improvement with specific carbohydrate diet in pediatric Crohn disease. *J Pediatr Gastroenterol Nutr* 2014;59:516–521.
51. Wahbeh GT, Ward BT, Lee DY, Giefer MJ, Suskind DL: Lack of mucosal healing from modified specific carbohydrate diet in pediatric patients with Crohn disease. *J Pediatr Gastroenterol Nutr* 2017;65:289–292.
52. Olendzki BC, Silverstein TD, Persuitte GM, Ma Y, Baldwin KR, Cave D: An anti-inflammatory diet as treatment for inflammatory bowel disease: A case series report. *Nutr J* 2014;13:5.
53. Sigall-Boneh R, Pfeffer-Gik T, Segal I, Zangen T, Boaz M, Levine A: Partial enteral nutrition with a Crohn's disease exclusion diet is effective for induction of remission in children and young adults with Crohn's disease. *Inflamm Bowel Dis* 2014;20: 1353–1360.

54. Aggarwal BB, Harikumar KB: Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. *Int J Biochem Cell Biol* 2009;41: 40–59.
55. Schneider A, Hossain I, VanderMolen J, Nicol K: Comparison of remicade to curcumin for the treatment of Crohn's disease: A systematic review. *Complement Ther Med* 2017;33:32–38.
56. Suskind DL, Wahbeh G, Burpee T, Cohen M, Christie D, Weber W: Tolerability of curcumin in pediatric inflammatory bowel disease: A forced-dose titration study. *J Pediatr Gastroenterol Nutr* 2013;56:277–279.
57. Hanai H, Iida T, Takeuchi K, *et al.*: Curcumin maintenance therapy for ulcerative colitis: Randomized, multicenter, double-blind, placebo-controlled trial. *Clin Gastroenterol Hepatol* 2006; 4:1502–1506.
58. Romano C, Cucchiara S, Barabino A, Annese V, Sferlazzas C: Usefulness of ω-3 fatty acid supplementation in addition to mesalazine in maintaining remission in pediatric Crohn's disease: A double-blind, randomized, placebo-controlled study. *World J Gastroenterol* 2005;11:7118–7121.
59. Lev-Tzion R, Griffiths AM, Leder O, Turner D: Omega 3 fatty acids (fish oil) for maintenance of remission in Crohn's disease. *Cochrane Database Syst Rev* 2014;2:CD006320.
60. Feagan BG, Sandborn WJ, Mittmann U, *et al.*: Omega-3 free fatty acids for the maintenance of remission in Crohn disease: The EPIC randomized controlled trials. *J Am Med Assoc* 2008; 299:1690–1697.