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Editorial Board Member of *World Journal of Gastroenterology*, Pankaj Garg, FASCRS, MBBS, MD, CEO & Chief Surgeon, Department of Colorectal Surgery, Garg Fistula Research Institute, Panchkula 134113, Haryana, India. drgargpankaj@gmail.com

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Examining dietary interventions in Crohn's disease

Lynna Chen, Ashish Srinivasan, Abhinav Vasudevan

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Lynna Chen, Ashish Srinivasan, Abhinav Vasudevan, Department of Gastroenterology and Hepatology, Eastern Health, Box Hill 3128, Australia

Ashish Srinivasan, Abhinav Vasudevan, Eastern Clinical School, Monash University, Box Hill 3128, Australia

Corresponding author: Abhinav Vasudevan, BMed, FRACP, Doctor, Department of Gastroenterology and Hepatology, Eastern Health, 8 Arnold St, Box Hill 3128, Australia. abhinav.vasudevan@monash.edu

Abstract

This editorial builds on the article by Shakhshir *et al.* We conducted an overview of evidence-based dietary interventions in adults with inflammatory bowel disease (IBD). In the IBD population, there may be a role for the Mediterranean diet due to its anti-inflammatory effects, long-term sustainability, and role in improving cardiovascular health. In active Crohn's disease, the use of exclusive enteral nutrition, the Crohn's disease exclusion diet, or the specific carbohydrate diet may be used as a short-term adjunct to medical therapy and may improve mucosal healing. The low-FODMAP diet can assist in reducing symptoms for patients without evidence of active bowel inflammation. As interest in nutritional therapy increases amongst clinicians and patients alike, it is integral that dietary therapies are understood and discussed in routine management of patients with IBD as part of holistic care, ideally through a multidisciplinary setting with involvement of experienced dietitians. This serves to improve clinician-patient engagement and reduce complications of IBD including micro and micronutrient deficiencies.

Key Words: Inflammatory bowel disease; Nutrition; Dietary therapies; Inflammation; Malnutrition

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Core Tip: Dietary therapies can be used to reduce inflammation or improve symptoms in patients with Crohn's disease. The Mediterranean diet has been associated with improved outcomes in inflammatory bowel disease (IBD), and potentially reducing its development. Exclusive enteral nutrition and Crohn's disease exclusion diet can be used for the induction of remission in Crohn's disease. Multidisciplinary management of patients with IBD should include dietary advice and the involvement of experienced dietitians.

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INTRODUCTION

This editorial comments on the article 'Global research trends on diet and nutrition in Crohn's disease' by Shakhshir *et al* [1]. Inflammatory bowel diseases (IBD), including Crohn's disease and ulcerative colitis, are chronic remitting and relapsing conditions of the gastrointestinal tract characterised by inflammation and an aberrant immune response[2]. The aetiology of IBD is postulated to involve a complex interplay between environmental and genetic factors[3]. Among the environmental factors, dietary factors have been implicated, including the use of dietary emulsifiers, poly-unsaturated fats, and ultra-processed foods[4,5]. Nutritional interventions are increasingly recognised as a critical component of comprehensive IBD care, encompassing strategies to mitigate disease symptoms, reduce inflammation, and correct nutritional deficiencies. Malnutrition is a significant concern in IBD patients due to factors such as poor gastrointestinal absorption, increased gastrointestinal losses, and a hypermetabolic state driven by chronic inflammation. These factors contribute to a high prevalence of micronutrient and macronutrient deficiencies, which can exacerbate disease related symptoms and impair patient reported quality of life[6,7].

As identified by Shakhshir *et al*[1], there is growing interest in dietary approaches in treating Crohn's disease with a steady growth of publications in this field, however, further knowledge is required to strengthen recommendations in nutrition management in IBD. Landmark dietary trials in paediatric populations have been extrapolated for use in adult populations, however the role of dietary therapies is less certain given the presence of more heterogenous disease phenotype and variability in lifestyles. Hence, an awareness of the role and effectiveness of dietary therapies in IBD remains integral in making evidence-based recommendations to patients for managing IBD. This editorial focuses on the role of diet in Crohn's disease in the adult population, as its efficacy in ulcerative colitis is less certain.

ROLE OF DIET IN PATHOGENESIS AND AETIOLOGY

The multifactorial aetiology of IBD involves a dynamic interplay between genetic predisposition, environmental factors, immune dysregulation, and gut microbiota alterations. Among these, diet has emerged as a crucial environmental factor influencing the development and progression of IBD.

Epidemiological studies have consistently shown that dietary patterns can influence the pathogenesis of IBD[4]. In fact, Western dietary patterns characterised by high intake of refined sugars, fats, and processed foods and low intake of fibre have been associated with an increased IBD risk and more active disease[4]. Conversely, diets rich in fibre, fruits, vegetables, and anti-inflammatory nutrients such as omega-3 fatty acids and vitamin D have been associated with a lower risk of IBD[8].

The role of short-chain fatty acids, such as butyrate; a product of fermentation of dietary fibres with anti-inflammatory properties, is hypothesised to play a role in maintaining intestinal barrier integrity and gut homeostasis[9]. Studies also show that patients with IBD have lower levels of faecal short-chain fatty acids[9,10]. Dietary fats, including polyunsaturated fatty acids and omega-6 fatty acids from animal protein, excluding eggs and dairy, have also been implicated in incident cases of IBD[11].

PATIENT AND CLINICIAN PERCEPTIONS

As a modifiable lifestyle factor, diet presents an attractive therapeutic option due to its potential to improve quality of life with fewer perceived side effects than medical therapy. Moreover, patients often proactively initiate dietary modification, including self-restrictive diets, to manage their symptoms. In large scale questionnaires, up to two-thirds of patients report avoiding foods they enjoy to help prevent relapse of IBD[12] and majority (85.4%) of patients believed that diet triggers relapses[13]. Similarly, 59% of patients valued nutrition to be at least as important as pharmacotherapy for the management of IBD, including 62% who believed diet to be more important in influencing the disease course[14].

In addition, nearly half (43.8%) of patients describe dietary modifications, whether self-adjusted or clinician prescribed, to have significant interference in their social life[15]. From the clinicians' perspective, diet is increasingly recognised as

an adjunctive treatment to pharmacotherapy, and dietitians can play a pivotal role in multidisciplinary management of IBD when they are available. The lack of high-quality trials and scarcity of practical resources can limit the use of dietary therapies, with only a limited number of gastroenterologists actively incorporating dietary counselling into clinical practice[16].

Further work is required to bridge the gap between patient and clinician perceptions towards dietary therapy in IBD. A cross-sectional study of 928 patients found that 61% of patients felt their IBD specialist disregarded the importance of diet in their management. Only 26% reported receiving dietary advice from their doctor despite nearly all (98%) gastroenterologists surveyed reporting providing advice[17].

A key strategy is the inclusion of an experienced dietitian as standard of care in IBD management. Dietitians play an important role in the assessment and can tailor individualised plans in approaching malnutrition management, instituting therapeutic diets and alleviating symptoms[18].

MEDITERRANEAN DIET

The Mediterranean diet (MD), characterised by high consumption of fruits, vegetables, whole grains, legumes, fish, and olive oil, and low intake of red meat and processed foods, is the hallmark of lifestyle modifications and diet therapy in cardiovascular and metabolic health. It is associated with lower levels of systemic inflammation and oxidative stress markers in the general population[19,20].

MD's dietary plan shares similarities with foods that have been implicated as protective factors and aims to avoid foods that have been implicated as risk factors for the development of IBD. A large-scale prospective cohort study has shown a lower risk of Crohn's disease onset (HR = 0.42, 95%CI: 0.22-0.80) in participants adherent to the MD, but not ulcerative colitis (HR = 1.08, 95%CI: 0.74-1.58)[21].

In patients with active Crohn's disease, the MD has shown similar rates of remission as induction therapy compared to the specific carbohydrate diet (SCD). A randomised trial involving patients with ileal (23.9%), colonic (17%), and ileocolonic (57.6%) disease showed 43.5% of the MD group achieving symptom remission at week 6, compared to 46.5% in the SCD group ($P = 0.77$). Faecal calprotectin response was not significantly different between the two groups (MD 30.8% *vs* SCD 43.88%; $P = 0.83$). Both diets were well tolerated, however adherence to a strict diet declined over time to 40% at week 12[22]. A randomised control trial of ulcerative colitis patients saw similar improvements in faecal calprotectin compared to an unrestricted diet (20% FC > 100 *vs* 75% FC > 100), with good tolerability[23].

EXCLUSIVE ENTERAL NUTRITION

Exclusive enteral nutrition (EEN) has emerged as a compelling therapeutic option in inducing remission and mucosal healing in Crohn's disease without several of the adverse effects associated with pharmacotherapy. EEN involves the exclusive consumption of a nutritionally complete liquid formula while eliminating regular solid food intake. Common regimes include a six to eight week period of exclusive use following which a normal diet is gradually reintroduced. The mechanisms by which EEN exerts its beneficial effects are hypothesised to be related to modulation of the gut microbiota, reduction of intestinal permeability, anti-inflammatory effects, and providing bowel rest which could contribute to mucosal healing[16,24].

Several clinical trials have established EEN as an effective first-line therapy for inducing remission in Crohn's disease. A randomised controlled trial by Borrelli *et al*[25] demonstrated that a polymeric diet was more effective than corticosteroids (79% *vs* 67%) in inducing healing in a paediatric population. Subsequent studies have supported these findings showing improvement in biochemical and endoscopic response rates and nutritional parameters without side effects[26-29].

In adult populations, the data is less robust and larger studies have not been able to recreate the same degree of efficacy. A meta-analysis demonstrated that EEN was not superior in efficacy to steroids as induction therapy in an adult population, with adverse events including nausea, vomiting, diarrhoea and bloating. Palatability and inability to tolerate EEN with symptoms of nausea, vomiting and fatigue were common reasons for withdrawal[30,31]. Early reports suggested greater efficacy with small bowel involvement whereas data on isolated colonic disease remains equivocal. Xu *et al*[32] described a 51.9% clinical remission rate in colonic Crohn's compared to 68.2% with ileal involvement.

Dissatisfaction with not being able to eat food, especially on social occasions, also contributed to poor adherence[33]. This highlights that the implementation of EEN can be challenging, and adherence can be difficult over extended periods.

EEN can also be used as a steroid-sparing therapy, including as an adjunctive therapy to optimise nutrition and reduce post-operative complications in malnourished patients prior to elective IBD related bowel surgery, or for refractory disease in conjunction with medical therapy[34].

CROHN'S DISEASE EXCLUSION DIET

The Crohn's disease exclusion diet (CDED) is a structured diet that aims to reduce gut inflammation by excluding certain foods known to exacerbate symptoms and possibly trigger immune responses and gut dysbiosis. This diet focuses on eliminating specific food components, such as gluten, dairy, processed foods, and certain additives, while encouraging

the consumption of fruits, vegetables, lean proteins, and other nutrient-dense foods.

A study of forty-four adults with mild-moderate Crohn's disease showed 57% clinical remission at week 6, and 68% when combined with partial enteral nutrition. Eighty percent of those in remission at week 6 maintained clinical remission at week 24, with 35% in endoscopic remission at the time[35]. Earlier paediatric studies demonstrated an increase in steroid-free remission in patients with CDED, with augmentation of the effect when partial enteral nutrition was added[24,36].

One of the key strengths of the CDED is its ability to provide balanced and adequate intake of essential nutrients unlike highly restrictive diets that may lead to nutritional deficiencies. The CDED is implemented in phases, allowing for gradual reintroduction of excluded foods. This phased approach helps in identifying specific dietary triggers and maintaining long-term adherence.

CDED provides a good alternative where there is intolerance to EEN with improved compliance (85% *vs* 63%)[35]. Consensus agreements recommend supplementation with enteral nutrition to meet nutritional requirements and diet reintroduction after 12 weeks of therapy to avoid malnutrition[37].

SCD

The SCD is a nutritional regimen that restricts the intake of complex carbohydrates, and promotes the consumption of monosaccharides, which are easily absorbed and purported to minimise microbial dysbiosis. It is based on the theory that certain carbohydrates are not completely digested and absorbed, leading to fermentation and growth of pathogenic bacteria in the intestines.

In the paediatric populations with Crohn's disease, studies have observed clinical and laboratory improvements following SCD therapy as well as significant changes in the faecal microbiome[38,39]. Use of the SCD has been shown to increase populations of beneficial bacteria and decrease inflammatory markers in a paediatric population with active Crohn's disease[40]. A randomised trial comparing SCD with the MD in adult patients with Crohn's disease found similar rates of early remission at week 6 (46.5% *vs* 43.5%) with a faecal calprotectin reduction in 34.8% and 30.8% respectively[22]. However, there are limited controlled studies comparing SCD to an unrestricted diet, limiting its widespread take-up as first-line dietary therapy in IBD.

Potential drawbacks from using the SCD long-term include its restrictive nature given elimination of sugars, high-lactose dairy and starchy vegetables.

LOW-FODMAP DIET

The low FODMAP diet, initially developed for the management of irritable bowel syndrome (IBS), has increasingly been examined for its potential benefits in patients with IBD. This dietary intervention focuses on reducing the intake of carbohydrates that are poorly absorbed in the small intestine and highly fermentable, potentially exacerbating symptoms like bloating, gas, and abdominal pain through luminal distension and altered gut motility[41]. Given the overlap in symptoms between IBS and IBD, particularly during quiescent phases of the latter, the low FODMAP diet has been considered a valuable nutritional approach for symptom management in IBD patients.

Low FODMAP diet was beneficial for symptom management in IBD, with approximately half of patients finding improvement in symptoms of abdominal pain, bloating, wind, and diarrhoea. Compliance can be a limiting factor in its widespread use and lower compliance has been associated with a lack of efficacy[42-44]. A systematic review of 319 patients in IBD (96% in remission) found a significant improvement in diarrhoea, satisfaction of gut symptoms, bloating, pain, fatigue; however did not improve constipation[45].

The role of the low FODMAP diet on long-term disease outcomes and inflammation remains under investigation and it currently cannot be recommended as a treatment of IBD but rather as an adjuvant treatment for symptomatic improvement. Furthermore, it may not be suitable for those with severe disease due to the risk of nutrient deficiencies and potential impact on disease activity. Its sustainability can be challenging due to its restrictive nature, with long-term adherence diminishing over time.

MICRONUTRITON and MACRONUTRIENTS

Reduced dietary intake due to anorexia, nausea, and abdominal pain, combined with malabsorption and increased metabolic demands, contribute to macronutrient and energy deficits. Comprehensive nutritional assessment, including regular monitoring of body weight, body composition, and laboratory markers of nutritional status, is essential for identifying and addressing nutrient deficiencies in IBD patients. The use of screening tools such as the Malnutrition Universal Screening Tool, Saskatchewan IBD-nutrition risk and Subjective Global Assessment can help clinicians identify at-risk patients and tailor nutritional interventions accordingly[46,47]. A cross-sectional study of over 200 patients with IBD found malnutrition rates of 27%-37%[48].

Iron deficiency is prevalent due to chronic intestinal bleeding, reduced iron absorption, and inflammation-induced alterations in iron metabolism. Routine screening allows for early detection, and management with intravenous iron therapy is shown to be more effective and better tolerated than oral iron[49,50]. Low vitamin D levels are associated with

increased disease activity and a higher risk of hospitalisation and surgery in IBD patients, highlighting the need for regular monitoring and supplementation[51]. A prospective study showed low micronutrient levels were common even in quiescent disease; vitamin D was the most common deficiency (29%), followed by zinc (16%), vitamin B6 (14%), vitamin C (13%) and vitamin B12 (11%)[52]. Folate and vitamin B12 deficiencies are also common, especially with ileal Crohn's or post-ileal resection[53]. Regular monitoring and supplementation of these vitamins were necessary to prevent anaemia and neurological complications.

CLINICAL IMPLICATIONS

The role of diet in IBD is increasingly recognised as an area of importance by clinicians and patients alike. This is an evolving field so there may be disparities in perceptions and attitudes toward diet between patients and clinicians which may partially relate to differences in how information is acquired. For example, patients may revert to social media, online forums, and patient advocacy groups for dietary advice while clinicians may rely on peer-reviewed journals, clinical guidelines, and professional societies for guidance. Improved awareness, communication and education, the development of evidence-based dietary guidelines, and the inclusion of dietitians in IBD care are integral steps in bridging this gap so that nutritional therapy can be optimised for patients with IBD.

CONCLUSION

Dietary therapies are an important element of IBD management. It can provide wide ranging benefits in improving nutritional outcomes, alleviating symptoms and sometimes improving inflammation. Evidence supports the integration of nutritional care into standard IBD management protocols, emphasising the need for multidisciplinary approaches that include dietitians and nutrition specialists. As further research and interest grows, integrating dietary knowledge and therapies in IBD care is adding to the potential strategies for optimising outcomes in IBD.

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Country of origin: Australia

ORCID number: Lynna Chen 0000-0002-7093-2036; Ashish Srinivasan 0000-0001-5952-1570; Abhinav Vasudevan 0000-0001-5026-9014.

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