

Conference on ‘Malnutrition matters’

Symposium 7: Nutrition in inflammatory bowel disease Dietary and nutritional considerations for inflammatory bowel disease

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Nutritional assessment and dietary advice are fundamental to inflammatory bowel disease (IBD) patient management and all patients should have access to a dietitian. Newly diagnosed patients often think that their pre-illness diet has contributed to the development of their IBD. However, epidemiological evidence to support diet as a risk factor is lacking. How the diet contributes to the gastrointestinal microbiota is interesting, although the role is not yet clearly defined. Nutritional problems in IBD are common. Malnutrition occurs in up to 85% of patients and weight loss affects up to 80% of patients with Crohn's disease and 18–62% of patients with ulcerative colitis. Nutritional deficiencies are prevalent, particularly in relation to anaemia and osteoporosis. Intestinal strictures can be problematic in Crohn's disease and limiting fibrous foods that may cause a mechanical obstruction in the gastrointestinal tract is helpful. Patients often explore dietary exclusion to alleviate symptoms but such changes may be self-directed or inappropriately advised and can lead to further nutritional deficiencies. Some patients experience concurrent functional symptoms (e.g. abdominal bloating, abdominal pain, flatulence and diarrhoea) that can significantly affect quality of life. Recently, a group of poorly absorbed carbohydrates that occur naturally in the diet called fermentable oligo-, di-, mono-saccharides and polyols have been associated with functional symptoms by intestinal bacterial fermentation leading to rapid gas production, and an osmotic effect increasing fluid delivery to the colon. Emerging evidence indicates that a diet low in fermentable oligo-, di-, mono-saccharides and polyols can alleviate functional symptoms in IBD.

Diet: Inflammatory bowel disease: Crohn's disease: Ulcerative colitis

Inflammatory bowel disease (IBD) is characterised by chronic intestinal inflammation with a relapsing and remitting nature. IBD comprises Crohn's disease (CD) and ulcerative colitis (UC). CD may occur anywhere within the gastrointestinal tract, most frequently affecting the ileum, and it is characterised by skip lesions with confluent deep linear ulcers, aphthoid ulcers, cobblestoning, granuloma, deep fissures, fistulae, strictures, fat wrapping, and is often rectal sparing⁽¹⁾. Clinical features include diarrhoea, abdominal pain, weight loss, malaise, anorexia or fever⁽¹⁾. UC is confined to continuous mucosal inflammation usually affecting the rectum and a variable extent of the colon without granuloma⁽²⁾. Depending on the extent and severity of disease,

symptoms include bloody diarrhoea, rectal bleeding and urgency⁽²⁾.

The aetiology of IBD is not fully understood but evidence indicates an immune dysfunction that is influenced by a genetic predisposition, the enteric microflora and environmental triggers^(3,4). Age, ethnicity and geographical location influence the rates of IBD with a modern Western lifestyle being positively associated^(5,6). Smoking has a significant role and childhood infections and diet have also been implicated⁽⁷⁾.

It is important to consider diet in terms of the aetiology of IBD but, due to the nature of the disease, diet and nutrition are also important to health during the disease

Abbreviations: CD, Crohn's disease, FODMAP, fermentable oligo-, di-, mono-saccharides and polyols; IBD, inflammatory bowel disease; LOFFLEX, low-fat fibre-limited exclusion; UC, ulcerative colitis.

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process in nutritional assessment, addressing nutritional deficiencies, as a potential treatment and also in the management of ongoing symptoms. All of the above require good access to dietetic services although there are inconsistencies in the quality of care that patients receive throughout the health service. This review will focus on all of these dietary and nutritional considerations for patients with IBD.

Does diet cause inflammatory bowel disease?

The gastrointestinal tract and enteric microbiota are in careful equilibrium with respect to immune tolerance but in IBD there is an immune dysfunction⁽⁸⁾. The modern Western diet is often implicated as an environmental factor involved in the aetiology of IBD⁽⁵⁾. Rates of IBD increased dramatically over the latter part of the 20th Century and particularly in developed countries⁽⁹⁾. Interestingly, increases in IBD rates have also been observed in countries where the diet is becoming more westernised (e.g. Japan and India) and in ethnic groups who move to a developed country and adopt a westernised diet^(5,6).

There are many challenges when studying diet as an aetiological factor in IBD. Case-control and cohort studies are often biased in their method of recruitment and selection of subjects, dietary assessment methods used and carrying out multiple comparisons⁽¹⁰⁾.

Numerous studies have reported a high intake of refined carbohydrate, particularly sugar, being associated with the onset of IBD⁽¹¹⁻¹⁵⁾. Recall bias in assessing dietary intake retrospectively is a major limiting factor in these studies, particularly as dietary changes often occur soon after symptoms develop which, in some, may be years before a diagnosis of IBD is confirmed⁽¹⁰⁾. Furthermore, these studies cannot demonstrate a causal mechanism in the development of IBD. A higher sugar intake is more likely to occur as a consequence of IBD due to altering the diet to alleviate symptoms. This may coincide with a corresponding decrease in the intake of dietary fibre⁽¹⁴⁾.

The immunomodulatory effects of PUFA are of great interest in the aetiology of IBD^(12,16). The *n*-3 PUFA, e.g. EPA and DHA, have anti-inflammatory properties, whereas the *n*-6 PUFA (e.g. arachidonic acid) have pro-inflammatory properties. Fish oil supplementation, rich in EPA and DHA, has been associated with a decrease in the production of inflammatory mediators, interferon- γ and PGE₂, in CD^(17,18). A high proportion of *n*-6 to *n*-3 PUFA in the diet has been reported in a Japanese study as possibly contributing to the development of CD⁽¹⁹⁾ and the use of margarine, which is typically high in *n*-6 PUFA, has been associated with the development of UC⁽²⁰⁾. The most compelling evidence to suggest that fat has a role in the aetiology of UC began with a European prospective cohort study that indicated a possible increased risk with a high intake of PUFA⁽²¹⁾. This was followed up with a nested case-control study from a cohort of 203 193 subjects where an increase in the intake of linoleic acid, an *n*-6 PUFA, was associated with the onset of UC⁽²²⁾. Participants who developed UC (*n* 126) were age and gender matched to four controls (*n* 504) and dietary data were compared.

Despite the high quality of the study design, the number of incident cases of UC is small and an association still needs to be verified for consistency with further studies.

There is a potential role for dietary protein to be linked to the aetiology of IBD⁽²³⁾. When undigested sulphur-containing proteins reach the colon, they are available for metabolism by the colonic microflora. The resulting end products may be toxic to the colon, for example, hydrogen sulphide. When hydrogen sulphide is exposed to nitric oxide, which is produced by anaerobic bacteria present in the colon, the barrier function of the colonic mucosa may be lost leading to immune dysregulation in UC. High intakes of animal protein have been reported in a prospective cohort study of 67 581 French women with 77 incident cases of IBD⁽²⁴⁾; however, another European prospective cohort study did not report similar findings⁽²¹⁾.

Other dietary factors have also been considered. A deficit in micronutrients may have a contributing role as studies of the pre-illness diet have reported a low consumption of fruit and vegetables⁽¹⁴⁾ and an increase in fast food⁽²⁵⁾. Another hypothesis involved dietary microparticles that are resistant to degradation in the gastrointestinal tract but can bind luminal biomolecules and act as adjuncts potentially stimulating an inflammatory cascade⁽²⁶⁾. However, removal of such microparticles from the diet did not facilitate disease remission in CD⁽²⁷⁾.

There is little conclusive epidemiological evidence to link diet in the causation of IBD. Perhaps the role of different types of fat warrants further investigation due to their immunological effects. More long-term epidemiological dietary studies are needed to identify what dietary habits and exposures may contribute. In addition, a better understanding of the gastrointestinal microbiota may provide some clues between diet and the aetiology of IBD.

Nutritional considerations during the disease process

The disease process of IBD leads to many nutritional challenges (Table 1) that can occur soon after diagnosis and during periods of remission as well as during relapses. Appetite and energy expenditure changes, possibly due to circulating inflammatory cytokines and malabsorption, affect nutritional status^(28,29). Appropriate dietary advice soon after diagnosis is an essential component of IBD care^(30,31). However, access to dietetic services is often limited⁽³²⁻³⁴⁾ and patients often seek advice from alternative and potentially less evidence-based sources⁽³⁵⁾ that can lead to patients following restricted diets that may detrimentally affect their nutritional intake^(36,37). Recent UK IBD service standards recommend that all patients with IBD should have access to a dietitian⁽³⁰⁾ and for a local population of 250 000 an IBD service should have a minimum of 0.5 whole time equivalent of a dietitian dedicated to gastroenterology⁽³⁰⁾.

Malnutrition is present in up to 85% of patients with IBD and weight loss occurs in up to 80% of patients with CD and 18-62% of patients with UC^(29,38). Patients with IBD should routinely have their BMI measured. Although a one-off measurement may not be particularly helpful as an indicator of lean body mass or nutritional status, particularly if it is in the healthy range or even

Table 1. Nutritional challenges in inflammatory bowel disease^(29,39,42,71,89)

Nutritional challenge	Possible causes
Weight loss and increased nutritional requirements	Extensive inflammation leading to nutrient malabsorption, high-output stoma or fistulae, inflammatory cytokines, poor appetite, short-bowel syndrome, surgery
Nutrient malabsorption	Bacterial overgrowth, bile salt malabsorption, extensive small-bowel disease, fructose malabsorption, inflammation, lactose malabsorption, multiple resections, short-bowel syndrome, surgery
Decreased dietary intake	Abdominal pain, dietary exclusion, fasting for investigations, intestinal obstruction, nausea, poor appetite, vomiting
Increased gastrointestinal losses	Diarrhoea, high output stoma or fistulae, inflammation, intestinal obstruction, nutrient malabsorption, vomiting
Anaemia	Blood loss, chronic disease, inflammation, poor dietary Fe intake
Fe deficiency	Blood loss, inflammation, poor dietary intake
Folate deficiency	Malabsorption, sulphasalazine
Vitamin B ₁₂ deficiency	Diarrhoea, disease activity in stomach, high-output stoma or fistulae, malabsorption, short-bowel syndrome, terminal ileal resection
Osteoporosis (Ca and vitamin D)	Corticosteroids, poor Ca intake, vitamin D deficiency
Mg deficiency	Diarrhoea, high output stoma or fistulae, malabsorption, short bowel syndrome
Zn deficiency	Diarrhoea, high-output stoma or fistulae, malabsorption, short-bowel syndrome
Electrolyte losses (e.g. Na and K)	Diarrhoea, high-output stoma or fistulae, short-bowel syndrome, vomiting

indicates overweight or obesity⁽³⁷⁾, if BMI is routinely measured, it helps generate a longer-term assessment of nutritional status. In addition, assessment of muscle function and micronutrient status are useful as these are often poor^(37,39). A recent study suggested that BMI and albumin levels are easy measurements to record for nutritional assessment but more detailed IBD-specific nutritional assessment criteria have not yet been developed⁽⁴⁰⁾.

Extra intestinal gastrointestinal losses, malabsorption, small-intestinal bacterial overgrowth, ileal resection and high-output stoma or fistulae can lead to Mg and/or Zn deficiency. This is particularly relevant for patients with CD where Mg and Zn deficiency have been reported in 14–33 and 3–5%, respectively^(41,42).

Osteoporosis

Patients with IBD have up to a 40% increased risk of fractures compared to the general population^(43,44). Osteoporosis is common in IBD occurring in 3–58% and 4–50% of patients with UC and CD, respectively⁽⁴⁵⁾. Increasing age, weight loss over 10%, BMI <20, malabsorption, poor Ca and vitamin D status, corticosteroid use and inflammation all contribute to the cause of osteoporosis⁽⁴⁶⁾. Important considerations include reducing the use of corticosteroids and assessing dietary intake of Ca and vitamin D, supplementing as appropriate, particularly as some patients restrict their intake due to avoiding dairy foods. The daily recommendation for Ca intake in IBD is 1000 mg⁽⁴⁶⁾. When corticosteroids are used for at least 12 weeks, patients should be given Ca and vitamin D supplementation⁽⁴⁷⁾ although there are arguments to supplement all patients receiving corticosteroids^(46,48).

Anaemia

Anaemia occurs in up to 67% and 74% of patients with UC and CD, respectively^(37,39,49). The causes are

multi-factorial with Fe deficiency and anaemia of chronic disease being the most common. Poor dietary Fe intakes⁽³⁶⁾ through avoidance of Fe-rich foods due to food aversions or intolerances may contribute to ongoing Fe deficiency but they are unlikely to be the only contributing factor to the anaemia in IBD⁽⁵⁰⁾.

In IBD, inflammation, Fe deficiency and anaemia of chronic disease often co-exist, making assessment of Fe status complex. Guidelines for diagnostic criteria and management have been developed and involve different cut-off levels for measuring Fe stores in the presence and absence of anaemia and inflammation^(51,52). Patients with IBD often develop gastrointestinal side effects to oral Fe and so these may not be helpful. Intravenous Fe may be warranted where supplementation is considered^(51,52).

Anaemia in IBD may also be caused by folate and/or vitamin B₁₂ deficiency resulting from a multitude of causes including increased nutritional requirements, reduced dietary intake, malabsorption or even medication used to treat IBD, particularly sulphasalazine⁽⁵³⁾. Folate and vitamin B₁₂ deficiency has been reported in up to 54% and 48% of patients with CD and 36% and 5% of patients with UC⁽⁴²⁾. Regular monitoring and oral supplementation (folate) or intravenous injection (vitamin B₁₂) may be required.

Diet in active disease

In the 1970s, total bowel rest and intravenous glucose was considered appropriate for patients with active disease but they soon developed protein-energy malnutrition. Parenteral nutrition overcame this issue^(54,55); however, it is invasive and carries more risks of serious complications and leads to gut atrophy arising from complete bowel rest. More recently, the enteral route has been considered more suitable if it is working and accessible. In children and adolescents, enteral nutrition is used a primary treatment for active CD^(56,57). Not only does it induce disease remission but it also improves nutritional status and helps with growth and development. In adults with CD, the

evidence for using enteral nutrition to induce disease remission is not so strong and it is less effective than corticosteroids^(56,57). In adults, enteral nutrition can be useful as an adjunctive treatment to other therapeutic measurements and particularly where the benefits of nutritional support are warranted⁽⁴⁷⁾.

Early enteral diets were based on an elemental formula but are often unpalatable due to the synthetic taste from free amino acids providing the source of nitrogen. More palatable peptide and whole protein formulas have been developed and are as efficacious as the elemental formula diets⁽⁵⁷⁾. The nutritional composition of enteral nutrition is an important consideration, particularly because of the immunomodulatory effects of fats. However, various studies have assessed different types of fats in enteral nutrition and to date no studies have identified what type of fat is most helpful^(58–61).

Enteral nutrition is usually prescribed from 10 d to 8 weeks. By 10 d there should be a clinical response and patients may even go into disease remission⁽⁶²⁾ but longer studies indicate that mucosal healing does not occur until later on and 8 weeks or more may be required^(63,64).

Enteral nutrition does not provide a primary therapeutic option in UC but can be used for nutritional support⁽⁶⁵⁾.

Maintenance of disease remission

In CD, the use of exclusion diets can be useful following a period of enteral nutrition^(66,67). One of the most successful exclusion diets is the low-fat fibre-limited exclusion (LOFFLEX) diet and it not only helps maintain disease remission⁽⁶⁷⁾ but it helps to identify potentially problematic foods that are poorly tolerated. There is an initial 2–4-week period where LOFFLEX foods are introduced to provide a nutritionally complete diet as quickly as possible, whereas the enteral diet is reduced and usually discontinued. A slow reintroduction programme then follows introducing a new food every 2–4 d to determine tolerance⁽⁶⁷⁾.

Supplementary enteral nutrition providing 35–50% of energy requirements using either an elemental or polymeric formula has been shown to help in the maintenance of disease remission if provided for up to 12 months⁽⁶⁸⁾.

In UC, patients often consider specific foods induce symptoms and self-restrict their diet⁽⁶⁹⁾. There is no evidence to support enteral nutrition in the maintenance of disease remission in UC.

Stricturing disease

Patients with stricturing disease should be advised to alter the dietary content of fibrous foods to prevent and alleviate obstructive symptoms⁽⁷⁰⁾. The degree of dietary strictness will be dependent on the nature (inflammatory and/or fibrotic) and extent (tightness and length) of the stricture. Typically high-fibre foods (whole grains, skins and pips in fruit and vegetables, nuts and seeds) and foods that are difficult to mechanically break down (e.g. gristle, skin on meat or fish) are avoided⁽⁷¹⁾. In some cases, patients may only be able to manage fluids without developing symptoms while others will manage a much wider variety of foods⁽⁷²⁾.

Probiotics and prebiotics

There is much interest in the role of the gastrointestinal microbiota and inflammation in IBD. Evidence for the pro-inflammatory and immune-regulatory effects is mounting⁽⁷³⁾. The potential therapeutic effects of probiotics and prebiotics have thus been investigated.

In patients with pouchitis, a multi-strain probiotic (VSL No. 3) appears to maintain remission^(74,75) and following pouch surgery help to prevent pouchitis⁽⁷⁶⁾. For maintenance of UC, a single-strain probiotic *Escherichia coli* Nissle 1917 is as effective as aminosalicylates^(77–79). Prebiotics have often been assessed in combination with probiotics and therefore it is difficult to determine their isolated effects⁽⁷³⁾. There is insufficient evidence for the use of probiotics or prebiotics to induce or maintain disease remission in CD^(73,80,81).

Functional symptoms in inflammatory bowel disease

It is well recognised that patients with IBD experience functional symptoms (e.g. abdominal bloating, abdominal pain, diarrhoea and flatulence) with estimates in the order of 33% and 57% of patients with UC and CD, respectively⁽⁸²⁾. It can be difficult to distinguish between whether symptoms are functional in nature or due to the ongoing inflammatory process. Functional symptoms can have a huge impact on patients' quality of life⁽⁸²⁾. Recent evidence supports a role for fermentable oligo-, di-, mono-saccharides and polyols (FODMAP) to contribute to the ongoing functional symptoms in susceptible individuals⁽⁸³⁾. FODMAP are poorly digested short-chain carbohydrates that increase fluid and gas production within the gastrointestinal tract. This process occurs in everyone and, in health, the gas and fluid are excreted without the onset of symptoms. However, in susceptible individuals the gas and fluid increases may lead to abdominal bloating, pain, flatulence, diarrhoea and urgency.

FODMAP have been shown to increase fluid output. In a single-blinded randomised crossover intervention study of a high FODMAP v. a low-FODMAP diet in ten IBD patients with an ileostomy, the low-FODMAP diet led to a significant decrease in daytime fluid output of 19% with $P = 0.01$ ⁽⁸⁴⁾. In addition, 32% of the FODMAP were recovered in the effluent in the high-FODMAP diet.

In another single-blinded randomised crossover intervention study in healthy volunteers and patients with irritable bowel syndrome assessing gas production, breath hydrogen was significantly higher following a high-FODMAP diet compared to a low-FODMAP diet⁽⁸⁵⁾. Interestingly, the patients with irritable bowel syndrome also reported an increase in symptoms after following the high-FODMAP diet but not the low-FODMAP diet⁽⁸⁵⁾.

A retrospective review of patients with IBD treated with a low-FODMAP diet indicates that overall functional symptoms and individual symptoms of abdominal pain, diarrhoea, bloating and wind were significantly better than before starting the diet⁽⁸⁶⁾. Although this is early work and a randomised controlled trial is warranted, FODMAP appear to induce functional gastrointestinal symptoms in susceptible individuals.

A low-FODMAP diet is complex, avoids a wide range of foods⁽⁸⁷⁾ and requires longer patient appointments and detailed written information to support the dietary advice⁽⁸⁸⁾. The diet originated in Australia and needs careful adaptation for use outside of Australia to include consideration of locally available fruit, vegetables and grains and local legislation on food labelling where high-FODMAP ingredients may be present in pre-packed foods.

Summary

There still remains no conclusive evidence that diet has a direct effect on the development of IBD. Advances in prospective cohort studies using high-quality dietary assessment methods will help to identify whether diet really does play a role. Nutritional assessment is central to identifying and treating nutritional problems during the disease process and the role of the dietitian cannot be under-estimated. Enteral nutrition continues to be a consideration for the management of active CD, more as an adjunctive treatment rather than a primary therapy. The introduction of a diet low in FODMAP shows some promising early data to improve functional symptoms in IBD. Further prospective work is needed to identify which patients may benefit from this approach.

Acknowledgement

The author declares no conflicts of interest. No funding was received.

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