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Nutritional consequences of chronic diarrhoea

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A B S T R A C T

There is an undeniable link between gastrointestinal disorders and malnutrition. Chronic diarrhoea is one of the most common gastrointestinal conditions that can impact a patient's nutritional status. The nutritional consequences will depend on the cause of the diarrhoea as well as the location and extent of gastrointestinal involvement. In general, malabsorption plays a central role in the interaction between malnutrition and chronic diarrhoea. Malabsorption can result in both nutritional deficits and diarrhoea. With severe malnutrition, chronic diarrhoea can persist due to impaired immune function and poor mucosal recovery. Food intolerance and an inappropriate diet in the setting of malabsorption may also contribute to chronic diarrhoea. Patients may attribute their gastrointestinal symptoms to specific dietary intake, which can lead to self-imposed indiscriminate dietary restrictions. Therefore, disease-specific treatment in conjunction with appropriate nutritional counselling and intervention is recommended in the prevention and treatment of malnutrition in patients with chronic diarrhoea. Specialized nutritional support through enteral or parenteral administration may be required to treat severe caloric and micronutrient deficiencies. In this review, we aim to summarize the mechanism, diagnosis, and treatment of the nutritional consequences of chronic diarrhoea.

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Introduction

Malnutrition in chronic diarrhoea covers a wide range of diseases that are associated with several overlapping nutritional consequences. The nature and severity of malnutrition depend on the cause of chronic diarrhoea as well as the location and extent of gastrointestinal involvement. The nutritional impact of chronic diarrhoea is best described in the paediatric literature. Starting in the 1960's, field studies in developing countries have demonstrated the negative impact of chronic diarrhoea on growth and development [1]. These studies were the first to correlate the severity of chronic diarrhoea with the anthropometric markers of malnutrition, such as stunting and muscle wasting [2–4]. It appears that chronic diarrhoea and malnutrition have a bidirectional causal relationship. Just as chronic diarrhoea predisposes to nutritional deficits, malnutrition increases the risk of having protracted diarrhoea due to general debility, poor immune response, and other adverse mucosal factors [5].

Chronic diarrhoea

Chronic diarrhoea was defined by a consensus statement of the American Gastroenterological Association as a reduction in fecal consistency lasting more than four weeks [6]. This definition has varied among different studies on chronic diarrhoea which complicates the extrapolation of prevalence data as well as the determination of actual causes and complications of chronic diarrhoea. There are a number of causes of chronic diarrhoea including: infectious etiologies, pancreatic disorders, intestinal diseases, endocrine-related causes such as hyperthyroidism, prior gastrointestinal surgeries, immune deficiencies, food intolerances, and medications, to name a few. In population-based studies, the leading causes of chronic diarrhoea will likely depend on the prevailing socioeconomic environment. In the United States, the common causes of chronic diarrhoea are due to irritable bowel syndrome, inflammatory bowel disease (including microscopic colitis), malabsorption syndromes (such as coeliac disease), and chronic gastrointestinal infections (giardiasis) [7,8].

Malnutrition

Malnutrition refers to an imbalance of nutritional intake and utilization. It is broadly used to describe undernutrition or inadequate nutritional intake. However, it also refers to overnutrition which is becoming an increasing public health problem by itself, in light of the growing prevalence of obesity [9]. Severe malnutrition is often used to describe protein-energy malnutrition which is still prevalent in many underdeveloped countries. In this review, malnutrition will refer to the nutritional deficits due to inadequate dietary intake or inability to maintain adequate bodily stores of calories and nutrients due to an underlying disease process such as chronic diarrhoea.

The prevalence of nutritional deficits from chronic diarrhoea is also unknown. To begin with, there is no reliable data on the prevalence of chronic diarrhoea among adults [6]. There is limited literature covering the different causes of chronic diarrhoea and their respective nutritional consequences. Our goal is to provide an overview of the nutritional consequences of chronic diarrhoea and their corresponding nutritional management. In addition, we will also discuss the indications for specialized nutrition support in patients with malnutrition from chronic diarrhoea.

Pathophysiology

In general, the causes of diarrhoea could be grouped based on the involved gastrointestinal organ such as the small and large bowels or other accessory digestive organs like the pancreas. When referring to digestive diseases, maldigestion and malabsorption are often inaccurately interchanged. Maldigestion simply refers to impaired hydrolysis of nutrients in the gastrointestinal tract. On the other hand, malabsorption specifically refers to defective mucosal absorption of nutrients primarily in the small intestine, which is the underlying process that results in both chronic diarrhoea and malnutrition. In due time, chronic diarrhoea may result in physical debility and increased nutrient

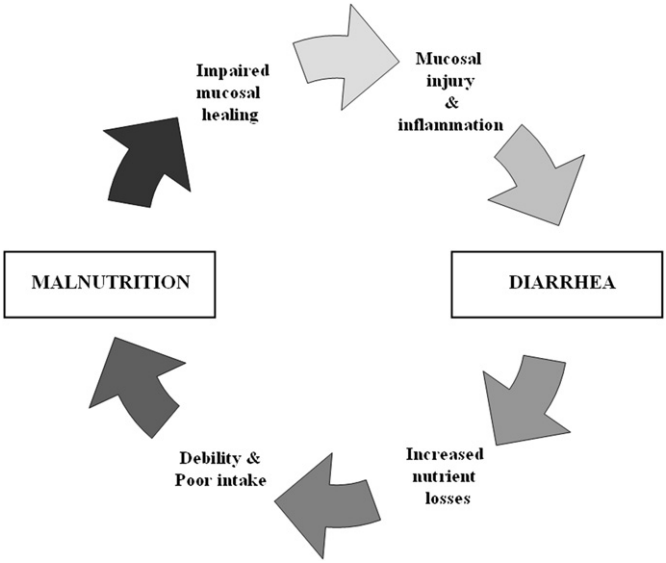

Fig. 1. Relationship between malnutrition and chronic diarrhoea.

losses. These lead to malnutrition which impairs mucosal recovery which can perpetuate the same cycle that led to malabsorption that caused both diarrhoea and malnutrition (Fig. 1).

The majority of macronutrients such as proteins, carbohydrates, and fats are absorbed in the duodenum and jejunum. On the other hand, the ileum is the only site for bile salt and vitamin B12 absorption. Knowledge of the location of macro- and micronutrient absorption in the small bowel is essential in understanding the nutritional consequences of chronic diarrhoea. The mechanisms of protein, carbohydrate, and fat malabsorption and their commonly-associated conditions that present with chronic diarrhoea are summarized in Table 1. The severity of both malnutrition and chronic diarrhoea will depend on the extent of small bowel involvement. In the setting of significant small bowel resection, the condition of the remaining small bowel and the presence of the colon in continuity with the small bowel will also influence the degree of nutritional deficits. In this review, we will present the nutritional consequences of the common causes of chronic diarrhoea.

Table 1
Mechanisms of macronutrient malabsorptions and their associated conditions.

Macronutrients	Mechanisms	Associated conditions with chronic diarrhoea
Carbohydrates	• Reduced disaccharides • Reduced mucosal surface	Lactose malabsorption Coeliac disease Post-infectious diarrhoea Short bowel syndrome
Proteins	• Increased mucosal permeability • Mucosal inflammation • Lymphatic obstruction	Inflammatory bowel disease Eosinophilic gastroenteritis Bowel ischaemia Coeliac disease Intestinal lymphangiectasia
Fats	• Pancreatic exocrine insufficiency • Mucosal inflammation	Chronic pancreatitis Cystic fibrosis Inflammatory bowel disease Coeliac disease

Nutritional consequences of chronic diarrhoea

Malabsorptive conditions

There are several gastrointestinal conditions that are associated with chronic diarrhoea and malabsorption. One of the common causes of malabsorption is coeliac disease. It is an immune-mediated inflammation of the small bowel as a result of exposure to gluten-containing food products in genetically-predisposed individuals. It involves the proximal small bowel with the classic histopathological findings of villous atrophy, increased intraepithelial lymphocytosis, crypt hyperplasia and chronic inflammation [10]. Treatment of coeliac disease requires strict life-long avoidance of gluten. In general, wheat, barley, and rye are avoided. For the first year after a diagnosis of coeliac disease is made, or in those with refractory symptoms, patients may be additionally instructed to avoid oats due to the risk of cross-contamination. The symptoms of coeliac disease in adults include steatorrhoea, abdominal pain, bloating, nausea, and weight loss. There are also many non-gastrointestinal manifestations of coeliac disease in adults such as: iron-deficiency anaemia, metabolic bone disease, arthritis, dermatitis herpetiformis, and neuropsychiatric symptoms [11–13]. Nonspecific gastrointestinal symptoms are often present in patients with coeliac disease secondary to malabsorption, resulting in nutritional deficits. In a survey of adult coeliac patients, 51% were found to have arm muscular area below the 15 % percentile, suggestive of malnutrition. However, 34% of the study participants admitted to poor adherence to gluten-free diet [14].

In untreated coeliac disease, common micronutrient deficiencies include folate, iron, calcium and vitamin D, vitamins A, B6, and B12. In brief, folic acid deficiency leads to megaloblastic anaemia. Iron deficiency results in microcytic anaemia, fatigue, headache, weakness and pica. Malabsorption of calcium and vitamin D may result in secondary hyperparathyroidism leading to decreased bone mineral density, osteoporosis, and osteomalacia [15]. Vitamin A deficiency can lead to night blindness. Vitamin B6 deficiency leads to cheilosis, glossitis, depression, and seizures. Diminished vitamin B12 levels results in megaloblastic anaemia with central and peripheral neuropathic changes. In patients with refractory coeliac disease, these nutritional deficits may be more profound. Refractory coeliac disease is defined by the persistence of villous atrophy and nutritional deficits despite more than 6–12 months strict adherence to a gluten-free diet [16]. Approximately 30–60% of patients with refractory coeliac may require parenteral nutrition due to severe malnutrition and weight loss [17,18].

Another cause of malabsorption is small intestinal bacterial overgrowth, which can present with abdominal pain, bloating, weight loss, and diarrhoea. Bacterial overgrowth occurs due to an excess of bacterial flora in the small bowel that is more representative of flora of colonic origin, with a predominance of gram-negative and anaerobic bacteria [19]. Bacterial overgrowth in the small bowel is defined as more than 10^5 organisms/ml [20]. There are many causes of small intestinal bacterial overgrowth including structural abnormalities (small bowel diverticula, blind loops, strictures), disorders with altered bowel motility (scleroderma, diabetes mellitus), conditions with diminished gastric acid (gastric resection or achlorhydria) and others (advancing age, coeliac disease, immunodeficiencies) [19].

Macronutrient malabsorption can occur with small intestinal bacterial overgrowth. The deconjugation of bile salts by intestinal bacteria can lead to fat malabsorption and secondary steatorrhoea. Early sugar fermentation in the small intestine can result in carbohydrate malabsorption, which is mediated by mucosal injury and reduced disaccharidases [21]. Like any malabsorptive condition, severe mucosal inflammation in the setting of small intestinal bacterial overgrowth can also contribute to protein malabsorption and iron deficiency [22,23].

In terms of micronutrient deficits, small intestinal bacterial overgrowth can result in low serum vitamin B12 levels due to premature cleavage of B12 from intrinsic factor and increased vitamin B12 consumption by anaerobic bacteria. Fat soluble vitamins (A, D, E, and K) may also have diminished levels due to fat malabsorption as discussed above [21]. In contrast, serum folate levels may be increased in small intestinal bacterial overgrowth due to microbial folate synthesis in the small bowel.

Aside from intestinal causes, exocrine pancreatic insufficiency can also result in malabsorption. This is often in the setting of chronic pancreatitis, which is a progressive inflammatory disease resulting in irreversible pancreatic dysfunction. Patients may present with abdominal pain and steatorrhoea. They often have signs and symptoms attributable to pancreatic exocrine and endocrine impairment. Nutritional

assessment in patients with chronic pancreatitis begins with obtaining a clinical history including dietary information, physical examination, anthropometric parameters, and a biochemical profile.

Fat malabsorption from exocrine dysfunction occurs when greater than 90% of pancreatic function is lost and pancreatic lipase release is less than 10% of normal [24]. As a consequence, patients with chronic pancreatitis are susceptible to fat-soluble vitamin (Vitamins A, D, E, and K) deficiencies. Vitamin B12 deficiency may result from decreased secretion of protease needed to release vitamin B12 from R protein (haptocorrin) which then allows it to complex with intrinsic factor for absorption in the terminal ileum. Metabolic bone disease is also common in patients with chronic pancreatitis due to multiple causes such as vitamin D and calcium deficiency and poor nutritional intake [25]. In patients who require nutrition support, post-pyloric enteral nutrition is the preferred route of feeding. However, parenteral nutrition may be administered if enteral nutrition is not effective due to refractory post-prandial pain, inability to maintain adequate calories, and continued weight loss [26].

Inflammatory bowel disease

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder of the digestive tract. Patients with IBD may experience diarrhoea, abdominal pain, nausea, vomiting, disorder of taste and decreased appetite, resulting to overall decreased nutritional intake. Based on the findings of abnormal biochemical and anthropometric measurements, it is estimated that 85% of IBD patients have protein energy malnutrition [27,28]. In addition, patients with IBD may experience increased energy expenditures due to chronic inflammation. Due to the chronic nature of the inflammatory condition, adequate protein intake should be assured in patients with active IBD. The recommended daily allowance for protein is 0.8 g/kg of actual weight. Patients with IBD without renal disease often require protein intake of 1.0–1.5 g/kg of body weight [29].

The absorption of vitamins may also be compromised in IBD patients, especially in those with Crohn's disease and significant ileal involvement. A summary of common vitamin and mineral deficiencies in IBD patients is presented in Table 2. Vitamin B12 and folate deficiencies are common in patients with Crohn's disease. Moreover, IBD patients are also predisposed to hyperhomocysteinemia compared to the general population [30]. Common signs and symptoms of B12 deficiency include megaloblastic anaemia, central and peripheral neural deficits, including cognitive changes, peripheral neuropathy, loss of position sense, and effects on the pyramidal tracts. Serum methylmalonic acid level is a sensitive early indicator of vitamin B12 status, and may be abnormal before the vitamin B12 level falls below normal values [31]. Treatment includes monthly intramuscular vitamin B12 injections, often at a dose of 1000 mcg [32]. Oral preparations are also available and may be effective with high doses of synthetic B12, but should not be relied upon in patients with conditions affecting normal absorption. Patients with folate deficiency may also manifest with megaloblastic anaemia, glossitis, and diarrhoea. Red blood cell folate is the most reliable measure of adequacy of tissue folate stores [33]. Folate replacement requires oral folate supplementation at 1–5 mg per day, and is of even greater importance in women of reproductive age with malabsorption.

Calcium and vitamin D deficiency in patients with Crohn's disease may result in decreased bone mineral density. Previously reported risk factors include: prolonged steroid use, malabsorption, and inadequate calcium or vitamin D intake. Signs and symptoms for vitamin D deficiency include bone pain, rickets, and muscle weakness. Hypocalcemia may present with osteoporosis or tetany. Serum 25-hydroxyvitamin D and calcium levels are used to assess vitamin D and calcium levels, respectively. The recommended supplementation of oral vitamin D replacement is 400–800 IU per day and calcium at 1000–1500 mg per day. Zinc deficiency can also occur in patients with IBD experiencing prolonged diarrhoea. Signs and symptoms of zinc deficiency include a flaky red rash on the face, groin and hands (acrodermatitis enteropathica), poor wound healing, dysgeusia, alopecia, and stunted growth in the paediatric population. Although not routinely used, lymphocyte and granulocyte zinc levels can be measured to accurately determine zinc levels in the body. In contrast, serum zinc levels are generally used in clinical practice instead.

IBD patients with gastrointestinal blood loss are more likely to have iron-deficiency anaemia resulting in microcytic anaemia, weakness, headache, and pica. Oral iron replacement is administered at 300–900 mg of elemental iron per day. Combining iron with vitamin C can increase the soluble

Table 2
Deficiencies in inflammatory bowel disease.

Micronutrients	Signs/symptoms of deficiency	Daily recommended replacement
Vitamins		
A	Increased risk of infection Corneal ulceration Night blindness	10,000–50,000 IU
B12	Megaloblastic anaemia Paraesthesia Ataxia	1000 mcg injection (monthly)
D	Hypocalcemia Osteomalacia Rickets	400–800 IU
E	Spinocerebellar disease Haemolytic anaemia Coagulopathy	30 IU
Folate	Megaloblastic anaemia Glossitis Diarrhoea	1–5 mg
Minerals		
Calcium	Cardiac arrhythmia Osteoporosis Tetany	1000–1500 mg
Iron	Microcytic anaemia Weakness Pica	300–900 mg
Magnesium	Muscle weakness Arrhythmia Seizures	600 mg
Selenium	Proximal muscle weakness Cardiomyopathy Connective tissue defects	60–100 mcg
Zinc	Delayed wound healing Immune dysfunction Diarrhoea	220–440 mg

nature of iron, aiding in its absorption. Hypomagnesaemia in IBD patients may occur as a complication of either gastrointestinal losses or decreased absorption. Signs and symptoms include arrhythmia, muscle weakness, and seizures. Oral replacement with magnesium gluconate is recommended at 600 mg of elemental magnesium per day. However, excessive magnesium supplementation may also cause or perpetuate diarrhoea.

Short bowel syndrome

Short bowel syndrome is a malabsorptive state that results from massive resection or loss of function of a significant portion of the small intestines. Etiologies include surgical resection from a vascular infarction, Crohn's disease, malignancy, and radiation enteritis [34]. The severity of short bowel syndrome depends on the length and integrity of the remaining small bowel, the segment of small bowel resected (jejunum vs. terminal ileum), and the presence or absence of the colon and ileocaecal valve. The small bowel can increase its absorptive capacity up to 400% [35]. The proximal bowel has a greater capacity for intestinal adaptation than the distal small bowel. Patients with resection of up to 50% of their small bowel have an increased chance of resuming an oral diet without the need for nutrition support. However, resections of 75% or more will require either temporary or permanent nutrition support [36].

The majority of macronutrients are absorbed in the first 150 cm of the small intestine. Vitamin B12 and bile salts are exclusively absorbed in the terminal ileum. Hence, resection of the ileum often results in vitamin B12 and altered bile salt absorption [35]. Resection of less than 100 cm results in increased

delivery of bile acid to the colon, leading to secretory diarrhoea. On the other hand, resection of more than 100 cm of terminal ileum results in decreased availability of bile salts due to the altered enterohepatic circulation, leading to decreased micelle production and fat malabsorption and maldigestion. As to the other parts of the small bowel, duodenal resection results in deficiencies in iron, calcium, and folic acid. Resection of the jejunum results in loss of disaccharides. Loss of the ileocaecal valve results in small bowel bacterial overgrowth which may lead to bile acid, fat, and vitamin B12 deficiencies. Resection of the colon along with loss of small bowel results in diarrhoea, which can lead to dehydration and electrolyte abnormalities. In patients with short bowel syndrome, the continuity of the colon with the remaining small bowel can also allow for carbohydrate salvaging, where the breakdown products of malabsorbed carbohydrates in the colon can aid in caloric needs.

Specialized nutritional support in the form of enteral or parenteral nutrition may be required in patients with short bowel syndrome to maintain normal nutritional status and prevent associated complications. An overview of the indications and administration of either enteral or parenteral nutrition support is presented at the later part of this review.

Gastrointestinal infections

Gastrointestinal infections are the most common causes of acute diarrhoea. Chronic gastrointestinal infections involving the small bowel can result in diarrhoea with significant nutritional consequences. Examples of these pathogens include: *Cryptosporidium*, *Cyclospora*, *Isospora*, *Giardia*, and *Strongyloides* [7]. Intestinal tuberculosis can also cause chronic diarrhoea and may sometimes mimic inflammatory bowel disease [37]. In general, these pathogens are difficult to eradicate in those with an immunocompromised states, HIV infection, or severe malnutrition. Acute gastrointestinal infections can also result in chronic diarrhoea with the development of post-infectious irritable bowel syndrome (IBS) which will be described in the next section. However, post-infectious IBS carries much less risk of malnutrition as compared to chronic infection.

Chronic infectious diarrhoea can result in malnutrition through several mechanisms [1]. Fig. 2 presents a diagram outlining the relationships between gastrointestinal infections, chronic diarrhoea, and malnutrition. It demonstrates a vicious cycle where infection directly contributes to malnutrition through increased catabolism and caloric losses. By indirect means, infection can induce mucosal injury

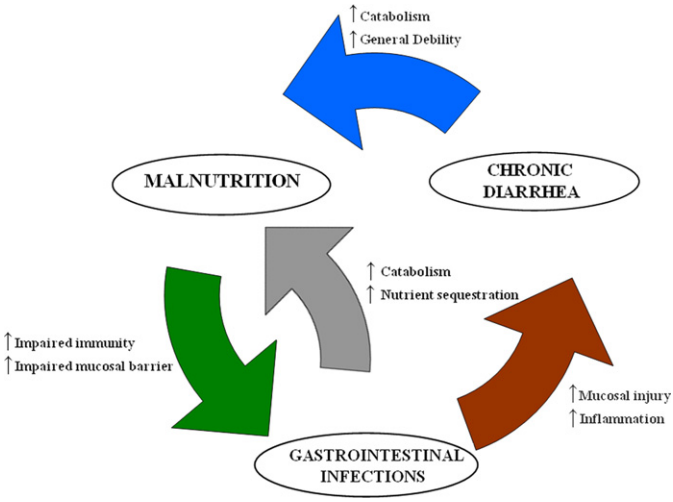

Fig. 2. Interaction between gastrointestinal infections and malnutrition.

and inflammation resulting in chronic diarrhoea. On the other hand, malnutrition can prolong the infection secondary to the impairment of the host's immune response and gut mucosal barrier.

Malabsorption in association with intestinal infections can result in increased calorie loss in the stool. Approximately 500 calories per day can be lost in the setting of diarrhoea [38]. Most of the calories wasted in stool come from dietary carbohydrate and lipid sources. A more severe form of malabsorption is protein-losing enteropathy with small bowel inflammation. In some instances, protein loss can be equivalent to 60% of the total albumin stores [39]. This can greatly impact the immune status and ability to heal mucosal injury. In severe cases of malabsorption, specialized nutrition support may be required to maintain adequate caloric and nutrient needs.

Vitamin B12 deficiency is the most common micronutrient deficit in infections involving the terminal ileum [40]. However, there are currently no guidelines for vitamin B12 supplementation in chronic infectious diarrhoea. The preferred route of vitamin B12 administration is by intramuscular injection especially if there is severe ileal disease. Deficiencies in fat soluble vitamins A, D, and E have also been reported in patients with chronic diarrhoea. In a survey of HIV patients with chronic diarrhoea, 30% have deficient plasma vitamin A levels [41]. Among the minerals, zinc deficiency was first reported in children with infectious diarrhoea. The World Health Organization recommends zinc supplementation for acute diarrhoea in children [42]. Zinc-fortified oral rehydration therapy has shown benefit in children with acute diarrhoeal illness. However, a recent meta-analysis demonstrated that zinc supplementation did not show statistically significant benefit in chronic diarrhoea [43].

Irritable bowel syndrome

Irritable bowel syndrome (IBS) is a common gastrointestinal disorder presenting with abdominal pain and altered bowel habits in the absence of an organic aetiology [44]. In contrast, bloody stools, large volume diarrhoea, and steatorrhoea usually suggest an organic cause apart from IBS. Functional diarrhoea is another condition that can cause chronic diarrhoea. It is separately classified from IBS in the Rome III criteria and it does not have the characteristic abdominal pain of IBS [45].

The prevalence of diarrhoea-predominant IBS is approximately 5% in the general population [12]. In spite of its prevalence, there are no studies estimating the burden of nutritional consequences from diarrhoea-predominant IBS. Clinicians recognize that diet is a major concern for IBS patients and yet there are only a few studies that have assessed their actual nutritional intake. There is a common assumption that IBS patients may avoid different food items as a means to cope with their symptoms. Nevertheless, food-induced symptoms and food intolerances may also confound the presentation of patients with diarrhoea-predominant IBS [46].

In one of the few studies on nutritional intake of IBS patients, there was no difference found in the average daily caloric intake of 188 IBS patients as compared to their age and gender-matched normal counterparts (2026 ± 532 kcal vs. 1990 ± 533 kcal, $p = \text{ns}$) [47]. This Swedish study suggests that IBS patients were similar to the general population in terms of meeting the recommended dietary guidelines. In addition, there was no difference either in the energy distribution from carbohydrate, fat or protein energy sources. There was also no difference in vitamin or mineral intake. However, dietary fibre intake was higher among IBS patients than their matched controls (19 ± 7 g vs. 16 ± 5 g, $p < 0.001$) [47].

Although the above findings are reassuring from a population-based perspective, nutritional deficits should be individually evaluated in IBS patients practicing self-imposed, selective food avoidance to cope with their symptoms. We recommend against broad, non-specific dietary restrictions. This approach may inadvertently restrict calorie or protein intake needlessly and may predispose patients to malnutrition [48]. A proven dietary approach to IBS symptoms is the elimination of short-chain carbohydrates [49]. These food items are collectively described by the acronym, FODMAPs (Fermentable Oligo-saccharides, Di-saccharides, Mono-saccharides And Polyols). Due to their poor absorption, these short-chain carbohydrates have considerable osmotic effects and gas-producing properties that exacerbate functional bowel symptoms. A description of the practical implementation of FODMAPs elimination diet has been described elsewhere for reference [49].

Nutrition support

Enteral nutrition

For patients with severe nutritional deficits in the setting of chronic diarrhoea who cannot sustain adequate nutrition through oral intake, nutrition support is a vital option to maintain and replenish nutrients. There are two routes of administration, through either enteral or parenteral means. Enteral nutrition refers to the provision of nutrients directly into the gastrointestinal tract via access with either a feeding tube or catheter [50].

The preference for enteral nutrition over parenteral nutrition support is based on the time-tested principle, 'if the gut works, use it'. There are several advantages of enteral nutrition over parenteral nutrition. Use of the gut enhances immune function in order to prevent infections. In contrast, gut disuse and absence of luminal nutrients have been demonstrated to increase mucosal permeability and disrupt the intestinal barrier [51]. Additionally, enteral nutrition is safer and more cost effective than parenteral nutrition [52]. It costs approximately 10 times less than that of parenteral nutrition, without accounting for the additional healthcare costs of complications from parenteral administration [53]. There are several complications associated with long-term administration of parenteral nutrition including catheter-related infections, cholestasis, bacterial overgrowth, and even nutrient deficiency [54]. With lower incidence of infections and other metabolic complications, enteral nutrition also results in shorter lengths of hospital stay [55].

Patients with chronic diarrhoea are at risk of chronic hypokalemia and acid–base disturbances. These patients are candidates for enteral nutrition as long as they have a functioning gastrointestinal tract. Some of the contraindications for enteral nutrition support in patients with malnutrition from chronic diarrhoea include: (a) severe short bowel syndrome with less than 100 cm of small bowel remaining, (b) intractable diarrhoea that is refractory to medical therapy, (c) high-output fistulas that are too distal to bypass with a feeding tube, (d) severe malabsorption, and lastly (e) previously failed enteral nutrition [56].

Once enteral nutrition support is initiated, monitoring is essential in assuring adequate nutrient delivery, especially if there is still ongoing diarrhoea. Patients on enteral feeding may also have worsening of their diarrhoea due to the following causes: (a) infection, (b) elixir medications which may contain sorbitol, (c) small intestinal bacterial overgrowth, (d) bolus feeding into the small bowel or too rapid a rate of infusion, and (e) suboptimal formula composition either from high osmolality concentrations, presence of lactose, or lack of fibre in the formula [57]. The need for enteral nutrition should be constantly reassessed, especially when the patient is able to sustain adequate oral intake with resolution of the underlying problem that predisposed them to malnutrition. For hospitalized patients, the American Society for Parenteral and Enteral Nutrition (ASPEN) has guidelines on the timing and process of terminating nutrition support [58].

Parenteral nutrition

Although enteral nutrition is clearly the preferred choice for nutrition support in patients with nutritional deficits from chronic diarrhoea, parenteral nutrition still remains as an alternative option when enteral nutrition is contraindicated or insufficient. Parenteral nutrition is recommended for the conditions previously mentioned, where there is a contraindication for enteral nutrition (see section on enteral nutrition). For patients with intestinal failure from short bowel syndrome, parenteral nutrition is essential for survival [59].

In parenteral nutrition, there are two routes of infusion, either central or peripheral. In central parenteral nutrition, the patient's full nutritional requirements are delivered into a large-diameter vein. In contrast, the peripheral venous delivery can only accommodate lower concentrations of nutrients which may not be sufficient for patients with significant malnutrition and large electrolyte needs [60]. In addition, the peripheral venous access will not be viable for a prolonged period of time.

Most patients with short bowel syndrome will require, at minimum, short-term parenteral nutrition to correct their nutritional and fluid imbalances. Oral intake is advised, once their volume, caloric, and electrolyte deficits have been stably corrected. They should receive adequate macro and

micronutrients to prevent energy malnutrition and other micronutrient deficiencies. The recommended maintenance is approximately 25–30 kcal per kg per day with 1.0–2.0 g per kg per day protein [29]. In addition to the parenteral formula, patients should receive sufficient fluid to prevent dehydration and acid–base disturbances, especially with ongoing diarrhoea.

We cannot overemphasize that long-term parenteral nutrition is costly and may result in serious complications. In spite of the reported improvements in the different biomarkers of nutritional status in parenteral nutrition, randomized trials have rarely shown improvement in general patient outcomes [61,62]. Among patients with chronic diarrhoea, those with severe short gut syndrome, medically-refractory Crohn's disease, and severe malnutrition have been shown to benefit from parenteral nutrition support [61–63]. The decision to start parenteral nutrition, especially long-term home parenteral nutrition, should be undertaken with a multi-disciplinary nutrition support service. We recommend following the specific guidelines for the initiation and administration of parenteral nutrition developed by ASPEN [64].

Future directions

The currently available literature on nutritional consequences of chronic diarrhoea is fragmentary and mostly devoted to individual disease entities. The extent of research on malnutrition in chronic diarrhoea is not at par with the actual burden of disease seen in clinical practice. Most of the current data that highlights the important connection between malnutrition and chronic diarrhoea are drawn from the paediatric literature which best exemplify the adverse effects of malnutrition through suboptimal growth and development. In terms of epidemiologic assessment, there is a lack of reliable data on the prevalence of malnutrition in chronic diarrhoea. In the area of pathophysiology, we have not fully explored the role of gut inflammation and its nutritional consequence [65,66]. Our understanding of the gut microbiota as it relates to both nutrition and diarrhoeal disease is still in its nascent stages [67]. There is also a requisite for outcomes research on the different nutritional interventions for malnutrition in the setting of chronic diarrhoea. There is no high quality evidence for most of the common empiric advice given to patients with chronic diarrhoea such as bland diets, avoidance of dairy products, and non-specific dietary fat restriction. In addition to these issues, there is also a clear need to evaluate the cost-effective approaches to the diagnosis and treatment of nutritional deficits in patients with chronic diarrhoea. Strategies on how to counteract commercial influence of fad diets and selective food restrictions without actual clinical indication will remain a challenge for clinicians caring for patients already at risk for malnutrition due to their chronic gastrointestinal conditions. Lastly, the opportunities for research are abundant, especially in view of the ageing population. The interplay between ageing, chronic gastrointestinal conditions and nutrition will be a fertile field for further study.

Summary

The complications of chronic diarrhoea still contribute to significant morbidity and mortality. Nutritional consequences of chronic diarrhoea should always be considered in addition to electrolyte loss and dehydration. The degree of malnutrition will depend on the extent of gastrointestinal involvement, and will vary with the different causes of diarrhoea and their adverse nutritional outcomes.

In this review, we presented the nutritional consequences of chronic diarrhoea. Gastrointestinal injury in the form of mucosal inflammation, damage, and villous atrophy can lead to malabsorption. Often, malnutrition in chronic diarrhoea involves a complex interaction between mucosal factors and the luminal environment as influenced by dietary habits and food choices. To be effective, any nutritional intervention will need to address both the underlying cause of the chronic diarrhoea and correction of its consequent nutritional deficits.

Conflict of interest

None.

Practice points

1. Knowledge of gastrointestinal anatomy and physiology is essential in understanding the nutritional consequences of chronic diarrhoea.
2. The severity of both malnutrition and diarrhoea will depend on the extent of small bowel involvement.
3. In the setting of small bowel resection, the condition of the remaining small bowel and the presence of a colon in continuity with the small bowel will also influence the degree of nutritional deficits.
4. Macronutrients such as proteins, carbohydrates, and fats are absorbed mostly in the duodenum and jejunum.
5. The ileum is the only site for bile salt and vitamin B12 absorption.
6. The underlying cause of the diarrhoea and its consequent nutritional deficits should be taken into consideration while implementing the nutritional intervention.

Research points

1. There is a lack of reliable epidemiologic data to assess the burden of malnutrition in patients with chronic diarrhoea.
2. Randomized controlled studies are needed to evaluate the efficacy of common dietary and nutritional interventions for malnutrition in the setting of chronic diarrhoea.
3. There is a need for cost-effectiveness studies for the diagnosis and treatment of nutritional deficiencies in chronic diarrhoea.
4. Emerging concepts on mucosal inflammation and gut microbiota should be investigated for their possible impact on malnutrition and chronic diarrhoea.

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