Nutritional management of the patient with Crohn's disease

Active Crohn's disease often co-exists with malnutrition and requires input from the inflammatory bowel disease multidisciplinary team in order to assess, prevent and treat the complications of both malnutrition and active disease.

The nutritional management of patients with inflammatory bowel disease and in particular Crohn's disease can be challenging even for the tertiary inflammatory bowel disease multidisciplinary team. Ensuring adequate nutritional intake in the hospitalized patient with Crohn's disease is important both in reversing any pre-existing malnutrition and also as a primary therapy for the underlying disease. This article attempts to de-mystify the nutritional assessment and management of these patients and explains the rationale for nutritional therapy as a sole therapeutic option. Hopefully this will empower the general physician to initiate early nutritional support for the Crohn's disease patient presenting to the acute medical take or general medical ward while the patient is awaiting specialist input from the inflammatory bowel disease multidisciplinary team.

Nutritional assessment

Crohn's disease is a chronic, relapsing, inflammatory condition of the gastrointestinal tract. Unfortunately the inflammatory burden, use of steroids and malabsorption as a result of disease activity leads to malnutrition in up to 75% of patients (Lochs et al, 2006a). As this figure is closer to 30% in whole hospital populations (McWhirter and Pennington, 1994), it is vital for these patients to have a prompt nutritional assessment at admission. The purpose of screening is multi-factorial but its benefits can be summarized as (Kondrup, 2003):

1. To avoid any deterioration in current clinical condition
2. To avoid the development of systemic complications of disease (for patients with Crohn's disease this is pivotal)
3. To improve recovery from illness
4. To reduce consumption of health resources, i.e. length of stay in hospital.

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Use of screening tools such the malnutrition universal screening tool (MUST) can be useful to identify those patients who will need prompt dietetic input and this basic screening tool has been validated for outpatient self-screening (Sandhu et al, 2015). Its ease of use means that assessment by a health-care professional during hospital admission should be straightforward. Patients with Crohn's disease who are deemed 'high risk' for malnutrition should be referred for a specialist dietician assessment which, if needed, can trigger collection of more detailed anthropological data (grip strength, mid-arm circumference, triceps skin fold measurement) to establish a comprehensive picture of nutritional status.

Unfortunately, a survey of current UK practice regarding nutritional screening and use of enteral nutrition in those with Crohn's disease found rather varied availability of dietetic services (Lomer et al, 2014). This has led to inconsistency in measuring nutritional status and while no reference was made to outcome data for those with increased availability of dietetic/nutrition services it has previously been shown that nutritional support improves mortality outcomes (Lochs et al, 2006b).

Nutritional support

Oral nutritional supplements

The first step for those with Crohn's disease deemed to be at risk should be to chart their nutritional intake. If they are not meeting their daily requirements they should be offered oral nutritional supplements. The European Society for Clinical Nutrition and Metabolism (ESPEN) has recommended up to 600 kcal/day in oral nutritional supplements in addition to regular food and these are generally well tolerated.

Enteral nutrition

If the number of calories required to supplement food intake is likely to be higher than 600 kcal/day or if the patient needs nutritional support for more than a short time then enteral nutrition delivered via a feeding tube should be considered. The formulation of feed is not pivotal with no difference in effect of elemental (amino

acid based), semi-elemental (oligopeptide based), and polymeric (whole protein) feeds (Lochs et al, 2006a). Nasogastric feeding is preferred in the absence of persistent vomiting or pyloric obstruction. This mode of feeding should initially be delivered via a continuous regimen as opposed to bolus aiming to reduce the risk of adverse events (Jones et al, 1980).

If a prolonged period of nutritional support is required then gastrostomy feeding should be considered. Historically, there has been some reluctance to consider gastrostomy tube feeding in this population because of the theoretical risk of tube site infection or persistent fistulous tracts following tube removal. This has not proved to be the case. Mahajan et al (1997) demonstrated a good safety profile in this patient population without increased incidence of peri-stomal infection or continued gastro-cutaneous fistula following tube removal. This was corroborated by Anstee and Forbes (2000), who demonstrated similar results, and this lead to international guidance advocating the safe use of enteral nutrition in this group (Lochs et al, 2006a).

Enteral nutrition as primary treatment

Beyond using enteral nutrition as a supportive therapy for those with Crohn's disease, there is also a well-established role for its use as a primary treatment. A meta-analysis (Zachos et al, 2007) has proposed that enteral nutrition can both induce and maintain remission in patients with Crohn's disease. This is a welcome finding as corticosteroids, which have been the mainstay for remission induction, subject the patient to increased risk of systemic complications such as bone loss, weight gain, diabetes mellitus and increased susceptibility to infection. Equally, corticosteroids have not be shown to provide a long lasting benefit with respect to mucosal healing (Rutgeerts, 2001).

A significant proportion of data advocating the use of enteral nutrition to treat Crohn's disease has come from paediatric populations where there are significant fears about long-term steroid side effects and particularly growth retardation. Use of intermittent enteral nutrition reduces the use of corticosteroids and also improves anthropometric data in paediatric patients (Belli et al, 1988); such findings have led to the recommendation that enteral nutrition is used first line to induce remission in children (Lochs et al, 2006a).

Exclusive enteral nutrition to induce remission in Crohn's disease

The role for induction of remission using enteral nutrition in adults with Crohn's disease has long been examined with some initial data from surgical patients awaiting operative intervention. Voitk et al (1973) observed that in 13 patients treated preoperatively with enteral nutrition for Crohn's disease there was an improvement in bowel-related symptoms and nutritional status, and a minority managed to avoid surgery. Observations like these in addition to enteral nutrition use in paediatric populations has led to extrapolations regarding enteral nutrition use in adult groups.

Since these initial findings, several randomized clinical trials with subsequent meta-analysis have sought to establish how exclusive enteral nutrition compares with corticosteroid for remission, with a Cochrane analysis undertaken by Zachos et al (2007). Difficulty arises when attempting to analyse data from this population because the studies have small patient numbers and heterogeneous patient characteristics, i.e. site of disease, age group, formulation of exclusive enteral nutrition and method of delivery of exclusive enteral nutrition. Despite this a significant benefit of corticosteroids over exclusive enteral nutrition was demonstrated (odds ratio 0.36, 95% confidence interval 0.23–0.56) with subsequent recommendations for clinical practice. An important factor in the reduced efficacy of exclusive enteral nutrition compared to steroids in adults with Crohn's disease is the large percentage of patients intolerant to exclusive enteral nutrition in some trials. A previous meta-analysis placed the proportion of adult patients with Crohn's disease who were intolerant of exclusive enteral nutrition at 37% (Fernández-Banares et al, 1995).

Steroids also have significant side effects, can impair mucosal healing and worsen outcomes if surgical input is needed (Rutgeerts, 2001). When the highest quality trials of exclusive enteral nutrition are considered, Borrelli et al (2006) demonstrated improved endoscopic remission rates in those receiving polymeric diets over those receiving corticosteroids (74% (95% confidence interval 51–89%) *vs* 33% (95% confidence interval 16–57%), $P<0.05$) and González-Huix et al (1993) demonstrated equivalence of enteral nutrition to steroids. Combining these data shows that there is no statistically significant difference between exclusive enteral nutrition and steroids for remission induction in Crohn's disease (odds ratio 1.18, 95% confidence interval 0.37–3.70), so the findings from the Zachos et al (2007) meta-analysis seem somewhat contradictory.

Implications for clinical practice

Enteral nutrition has its place for inducing remission in Crohn's disease but patient selection is important. It should be considered for patients with Crohn's disease who:

1. Present with continued symptoms of active disease that are established on pharmacological therapy
2. Have already recently received repeated courses of steroids in an attempt to achieve remission
3. Are at risk of becoming malnourished as a result of active disease.

It is generally accepted that enteral nutrition is continued for 6–8 weeks with gradual re-introduction of normal diet but what is less clear is which particular formulation should be used (Zachos et al, 2007).

Formulation of enteral nutrition

The implication of diet in the pathogenesis of Crohn's disease has derived from observations of mucosal healing when switching from normal diet to enteral nutrition but the exact mechanisms underlying this effect are not known. Theories include alteration of the gut microbiota and variation in combinations of fat, triglyceride and anti-inflammatory agents (such as transforming growth factor beta) in the enteral nutrition, leading to reduced antigenicity of gut contents with the extrapolation that the more simple the formulation the greater the benefit (Fell, 2005; Richman and Rhodes, 2013).

A meta-analysis (Zachos et al, 2007) compared remission induction rates across the range of enteral nutrition formulations. Analysis of ten trials including 188 adult patients treated with elemental diet and 146 adult patients treated with non-elemental diet (oligopeptide or polymeric) showed no statistically significant difference between the two groups (odds ratio 1.10, 95% confidence interval 0.69–1.75). This study also undertook a sub-group analysis looking for a difference in remission rates for feeds based on fat content (low (<20 g) fat/1000 kcal *vs* high (>20 g) fat/1000 kcal) and long chain triglyceride content (low (<10%) long chain triglyceride *vs* high (>10%) long chain triglyceride). Again no significant differences between the formulations were found with odds ratio 1.13 (95% confidence interval 0.63–2.01) and 1.39 (95% confidence interval 0.78–2.48) respectively.

Elemental diet can have an anti-inflammatory effect in Crohn's disease through altered cytokine production (Yamamoto et al, 2005) but the exact therapeutic mechanism of this remains unclear. Reducing the inflammatory burden by using such an elemental feed (perhaps reducing antigenic load) has been shown to be no better than using a whole protein-(casein) based formula rich in transforming growth factor-beta (e.g. Modulen IBD). Therefore when using enteral nutrition as a primary therapy in Crohn's disease the authors suggest selecting a formulation that is likely to be more palatable for the patient. This most often means using whole protein enteral nutrition which can be easily flavoured.

Enteral nutrition to maintain remission in patients with Crohn's disease

The utility of enteral nutrition for maintaining remission in patients with Crohn's disease is not clear. Non-randomized clinical studies have demonstrated some benefit in prolonging remission when combining enteral nutrition with 'normal diet' (Koga et al, 1993; Wilschanski et al, 1996; Verma et al, 2000). In terms of high quality studies, there have been only two randomized controlled trials in this field which were highlighted in a systematic review (Akobeng and Thomas, 2007).

Verma et al (2001) evaluated elemental *vs* polymeric feed by virtue of ability to reduce steroid dependency. In addition to their normal diet, patients were randomized to either elemental or polymeric nutrition orally with this making up 35–50% of their pre-study calorie intake. Steroids were withdrawn as enteral nutrition was continued and the primary outcome was 'treatment success' (defined as Crohn's Disease Activity Index <200, increase of <100 from baseline). At the end of the 12-month study period, six patients had withdrawn as they were unable to tolerate the enteral nutrition because of taste (all from the elemental group) and there was no difference between the groups in terms of achieving the primary end point (odds ratio 0.97, 95% confidence interval 0.24–3.92).

The second study by Takagi et al (2006) demonstrated over a 2-year follow-up period that relapse rates in patients with Crohn's disease in remission were significantly lower for those receiving a half elemental diet (34.6% *vs* 64.0%, multivariate hazard ratio 0.40, 95% confidence interval 0.16–0.98) than for those on an unrestricted diet.

Implications for clinical practice

There are a very limited number of small, randomized studies to guide the use of enteral nutrition in this scenario and the heterogeneity of the two best studies makes meta-analysis impracticable. The study by Verma et al (2001) compares one type of enteral nutrition with another and therefore does not really help to address the question of efficacy *vs* normal diet. Lastly there are no head-to-head studies comparing enteral nutrition with immunomodulators or biological treatments such as anti-tumour necrosis factor agents.

So in what scenarios can we envisage enteral nutrition being used to maintain remission? Those with supporting data suggested by Donnellan et al (2013) include:

1. The use of enteral nutrition postoperatively as a result of high recurrence rates in Crohn's disease (Rutgeerts et al, 1990). Perhaps those post-surgical patients not wanting to take immunomodulators may want an alterative therapy
2. Enteral nutrition as an adjunct to immunomodulators and biologics.

It is difficult for the authors to advocate the use of exclusive enteral nutrition to maintain remission in patients with Crohn's disease beyond these scenarios, not least because of the paucity of available data and issues with long-term compliance.

Parenteral nutrition

Indications for the use of parenteral nutrition can be challenging even for specialist inflammatory bowel disease units. Specialized nutrition support teams usually guide its use but it is helpful for the non-specialist to understand the indications for using parenteral nutrition.

Parenteral nutrition as primary treatment

The routine use of parenteral nutrition as primary treatment to either induce or maintain remission of Crohn's disease is not recommended (Van Gossum et al, 2009). This is the result of a lack of high quality data – the only prospective study comparing parenteral nutrition, enteral nutrition and oral food failed to demonstrate benefit for parenteral nutrition and 'bowel rest'.

There are specific circumstances where parenteral nutrition has a role and these primarily include those in the perioperative period and those with complex Crohn's disease where enteral nutrition cannot be used to maintain nutrition.

Perioperative phase

ESPEN gives fairly explicit guidance that parenteral nutrition can be considered for any surgical patient, including those with Crohn's disease. Its use is advocated in the perioperative phase to prevent or treat malnutrition before surgery and to improve postoperative outcomes.

Complex Crohn's disease and intestinal failure

Patients with complex Crohn's disease can have difficulty maintaining nutrition via the enteral route in a number of circumstances and may well have developed intestinal failure. This has led to guidance being issued recommending the use of parenteral nutrition in the following situations (Van Gossum et al, 2009):

1. Obstructed bowel not amenable to feeding tube placement beyond the obstruction
2. Short bowel resulting in severe malabsorption or fluid and electrolyte loss, which cannot be managed enterally
3. Severe dysmotility which makes enteral feeding impossible
4. A leaking intestine from high output intestinal fistula, or surgical anastomotic breakdown
5. Patient intolerant of enteral nutrition whose nutrition cannot be maintained orally
6. Unable to access the gut for enteral feeding.

Intestinal failure has been classified into three types (Lal et al, 2006). Type 1 intestinal failure is recognized as a transient phenomenon in the postoperative phase with development of an ileus and this can require short-term parenteral nutrition. Type 2 intestinal failure represents those Crohn's disease patients with complex disease with ongoing septic or metabolic consequences. Type 3 intestinal failure represents a cohort of more stable patients on long-term parenteral nutrition. It is beyond the remit of this article to discuss the nutritional management of these patients in detail but they will require a multidisciplinary approach to their nutritional care and are usually managed via a specialist nutrition support team for longer term parenteral nutrition.

Dietary modification

Having induced remission through enteral nutrition patients will want to return to a 'normal' diet in the longer term, as sole enteral nutrition is rather unpalatable for long periods. Consequently a number of different dietary modifications have been evaluated to maintain remission and control symptoms in patients with Crohn's disease but it remains unclear whether altering diet in this context actually helps patients through mucosal healing or if it primarily affects additional 'functional' symptoms.

Several diets such as 'elimination-reintroduction', 'low fibre, fat limited exclusion', and a diet low in fermentable, oligo-, di-, monosaccharides and polyols (FODMAP) have been evaluated by earlier reviews (Donnellan et al, 2013; Richman and Rhodes, 2013). These methods revolve around the principle that the normal diet is reintroduced slowly with single food types one at a time. This allows foods that cause symptoms to be identified. This method can be effective but is likely to place a large time burden on dietetic services that are already stretched and is primarily an adjunct to treatment with more robust trial data.

Interestingly, a diet low in FODMAPs, which is used in those with irritable bowel syndrome, was reported by Donnellan et al (2013) to improve symptom scores in those with Crohn's disease. FODMAPs are thought to be highly fermentable by gut bacteria, leading to gaseous distension and hence more gut-related symptoms in those with the predisposition, i.e. irritable bowel syndrome. It is likely that this diet achieves symptomatic reduction through a reduction in gaseous distension and osmotic load as opposed to direct effects on mucosal healing.

Conclusions

Malnutrition is common among patients with Crohn's disease and admission to hospital should prompt screening using a validated screening tool, i.e. MUST, with referral to dietetic services where indicated.

Where nutritional support is required, the enteral route is the preferred option, with oral nutritional supplements and tube feeding used in the appropriate setting in line with published guidance.

Enteral feeding can be used to induce remission but enteral nutrition is unlikely to become the primary treatment option for patients with active Crohn's disease. Patients with mild flares, poor baseline nutritional status and those with multiple previous courses of steroids should be considered for enteral nutrition to induce remission. The formulation of enteral nutrition is not important as there are no robust data on this topic but polymeric feeds are usually better tolerated by patients.

With regards to maintaining remission, practically there is little role for enteral nutrition not least because of the poor tolerability of long-term enteral nutrition but there are also limited data to support it use. Dietary

modification can help with symptom control. It is unlikely with the specific diets evaluated that there is a direct effect on mucosal healing but rather an amelioration of associated 'functional' symptoms.

There is no role for parenteral nutrition as primary therapy for Crohn's disease outside the limited scenarios outlined above. Specifically, perioperative use to optimize nutritional status for those who have failed to establish enteral nutrition, and those with intestinal failure provide the best rationale for use of parenteral nutrition.

The dietary management of patients with Crohn's disease is complex but is a common clinical scenario in the acute hospital setting. This article has guided the reader through the options and evidence for managing these patients, helping the general physician feel more confident with the nutritional management of Crohn's disease. **BJHM**

Conflict of interest: none.

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KEY POINTS

- Malnutrition is common among the Crohn's disease population and admission to hospital should prompt screening using a validated screening tool.
- Patients with Crohn's disease who are deemed 'high risk' for malnutrition should be referred to for a specialist dietician assessment.
- Where nutritional support is required, the enteral route is the preferred option.
- Enteral feeding can be used to induce remission in patients with Crohn's disease but enteral nutrition is unlikely to become the primary treatment.
- The routine use of parenteral nutrition as primary treatment to either induce or maintain remission of Crohn's disease is not recommended.
- Dietary modification can help with symptom control.