



Dietary treatment of irritable bowel syndrome

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Accepted 22 November 2014

Abstract

Introduction: Food is a recognized trigger for most patients with irritable bowel syndrome (IBS). In recent years, an emerging evidence base has identified dietary manipulation as an important therapeutic approach in IBS.

Sources of data: Original and review articles were identified through selective searches performed on PubMed and Google Scholar.

Areas of agreement: Randomized controlled trials have supported the use of a diet that restricts a group of short-chain carbohydrates known collectively as fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs). There is evidence that specific probiotics may improve symptoms in IBS.

Areas of controversy: The role of a high-fibre diet remains subject to ongoing debate with a lack of high-quality evidence. The long-term durability and safety of a low FODMAP diet are unclear.

Growing points: A paradigm shift has led to a focus on the relationship between diet and pathophysiological mechanisms in IBS such as effects on intestinal microbiota, inflammation, motility, permeability and visceral hypersensitivity.

Areas timely for developing research: Future large, randomized controlled trials with rigorous end points are required. In addition, predictors of response need to be identified to offer personalized therapy.

Key words: irritable bowel syndrome, diet, FODMAP, carbohydrate, fibre, gluten, probiotics

Introduction

Irritable bowel syndrome (IBS) is one of the commonest diagnosed gastrointestinal conditions. It can be subclassified according to the ROME III criteria for functional gastrointestinal disorders.¹ This categorizes patients according to the predominant stool type: diarrhoea predominant (IBS-D), constipation predominant (IBS-C), mixed (IBS-M) or unsubtyped (IBS-U). A positive diagnosis of IBS can be made using symptom-based criteria; however, it is important to exclude any gastrointestinal alarm symptoms such as weight loss, rectal bleeding, onset after 50 years of age, family history of colorectal cancer and an abdominal mass. In addition, it is prudent to send serology to exclude coeliac disease which is common and can mimic the symptom complex of IBS.

The majority of patients with IBS report that food can trigger gastrointestinal symptoms.² There is a high frequency of perceived food intolerance in patients with IBS, and as a result, dietary manipulation is a commonly adopted self-management strategy.³ The lack of quality evidence has historically limited the use of dietary therapies in clinical practice. However, in recent years, an evidence base has grown to support dietary manipulation as a therapeutic approach.

FODMAPS/Carbohydrate

The most compelling evidence exists for a diet that restricts a group of short-chain carbohydrates known collectively as fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs).⁴ They include fructo-oligosaccharides (FOS), e.g. wheat, galacto-oligosaccharides (GOS), e.g. legumes, lactose, fructose and polyols, e.g. sorbitol (a commonly used sweetener). FODMAPs are incompletely absorbed in the small bowel; rapid fermentation of these substrates leads to gas production and increased luminal water content secondary to an osmotic effect.⁵ The net result is luminal distention that may account for symptoms in patients with IBS.

A general reduction in carbohydrates demonstrated positive results in a prospective observational study involving 13 participants with moderate to

severe diarrhoea predominant irritable bowel syndrome (IBS-D). Participants were provided a 2-week standard diet and then 4 weeks of very low carbohydrate diet (VLCD); 77% reported adequate relief of symptoms during the VLCD, and abdominal pain scores were significantly improved.⁶

Restriction diets for fructose and sorbitol have demonstrated efficacy in a number of uncontrolled observational studies in patients with functional gastrointestinal disorders.⁷⁻⁹ A retrospective study demonstrated the efficacy of a fructose-/fructans-restricted diet in 62 patients with IBS and fructose malabsorption.¹⁰ Followed up over a median duration of 14 months, 74% of patients demonstrated a positive response to all abdominal symptoms (defined as an improvement by at least 5 points on a -10- to 10-point scale) with a relatively high adherence rate of 77%. However, a clear limitation of this study was its uncontrolled and retrospective design. A subsequent randomized, double-blinded, quadruple-arm, placebo-controlled, re-challenge trial involving 25 patients with IBS and fructose malabsorption who had previously responded to a low FODMAP diet added evidence that restriction of fructose and fructans was responsible for the associated symptom improvement.¹¹ Twelve patients had IBS-D, five had IBS-C and eight had alternating bowel habits. Participants were re-challenged with escalating doses of fructans, fructose, fructose/fructans mix and glucose (placebo) which were administered as drinks three times a day. Symptoms scores based on a 100-mm visual analogue scale were significantly higher in the fructose, fructans and fructose/fructans mixture arms compared with glucose. In addition, the symptoms were dose dependent.

Moreover, the FODMAP hypothesis was supported by a randomized, single-blinded, crossover intervention trial involving 15 healthy controls and 15 patients with IBS determined by the ROME III criteria where participants received a high and low FODMAP diet for 2 days with a 7-day washout period.¹² In terms of IBS subclass, four had IBS-D, seven had IBS-C, two had IBS-M and two had IBS-U. Higher levels of hydrogen were excreted in breath testing with the high FODMAP diet in normal controls and to a greater extent in IBS patients. The high

FODMAP diet was associated with an increase in gastrointestinal symptoms and lethargy in the IBS subgroup.

A UK-based, non-randomized study compared a low FODMAP diet with a standard national dietary advice provided by the National Institute for Health and Clinical Excellence (NICE) guidelines for IBS. ROME III criteria were not used and instead IBS was defined using NICE criteria (abdominal pain or bloating or discomfort or change in bowel habit for at least 6 months). Patients consecutively attended a follow-up dietician outpatient clinic; 43 patients received low FODMAP advice while 39 received standard advice (e.g. having regular meal times, restricting caffeine/alcohol, adjusting fibre intake). Patients in the low FODMAP group had a significantly greater improvement in composite symptom scores and more patients reported an improvement in bloating, abdominal pain and flatulence.¹³

Further to this, a small randomized controlled trial compared a habitual diet with a low FODMAP diet for 4 weeks in 41 patients with IBS.¹⁴ IBS was defined using ROME III criteria. Those with bloating and/or diarrhoea were included. Patients with constipation predominant IBS were excluded. At follow-up, there was a reduction in overall symptoms with lower severity scores for bloating, tiredness and flatulence in the intervention group. A major limitation in the study was the absence of blinding of diets to participants, and a degree of response in the intervention group could be attributed to a placebo effect.

A recent randomized controlled, single-blinded, crossover trial involved 30 patients with IBS and 8 healthy controls.¹⁵ The IBS participants were sub-classified according to ROME III criteria: 10 had IBS-D, 13 had IBS-C, 5 had IBS-M and 2 had IBS-U. Participants were randomly allocated to a 3-week diet low in FODMAPs or a typical Australian diet, with crossover after at least 21 days where their usual diets were consumed; the second interventional diet was not commenced until symptoms returned to a baseline level. Strengths of the study included the provision of all food by the investigators and blinding of the diets to participants. Global gastrointestinal symptoms were almost halved including subjects across all four subtypes of IBS, and individual

symptoms (bloating, abdominal pain and passage of wind) were significantly reduced while on the low FODMAP diet while no significant change was reported among healthy controls. A significant reduction in dissatisfaction with stool consistency was observed in both the IBS-C and IBS-D subtypes; the IBS-U and IBS-M groups were too small to analyse. In addition, adherence rates were noted to be high; 80% of IBS participants and 100% of controls were adherent to the low FODMAP diet using the authors definition as compliance for at least 17 of the 21-day diet.

There is now high-quality evidence to support the use of a low FODMAP diet as an effective intervention for the reduction of gastrointestinal symptoms in patients with IBS. The key studies are outlined in Table 1. An important concept is that the FODMAP hypothesis involves a general restriction of carbohydrates in contrast to previous empirical individual elimination diets. Detailed practical accounts of implementing the low FODMAP diet have been described elsewhere.^{16,17} The diet has only been evaluated in trial settings where it has been delivered by a specialist dietician and alternative forms of patient education have not been studied. Its efficacy in clinical practice needs to be determined where similar levels of dietician input may not be as readily accessible and long-term adherence rates may not be as high. Larger long-term studies are required to investigate whether effects are durable, identify predictors of response to the diet and determine the safety of the restricted FODMAP approach.

Fibre

Traditionally, a high-fibre diet has been recommended to patients with IBS, although its role remains subject to ongoing debate with a lack of high-quality evidence and contradictory data. The vast majority of evidence relates to fibre supplements with little evaluation of increased dietary intake from regular foods.

A Cochrane review completed in 2011 evaluated 12 randomized controlled trials of bulking agents (total 621 patients included) and found no beneficial effect with either soluble or insoluble fibre over

Table 1 Summary of key studies supporting the use of a low FODMAP diet

Study design	Participants	Outcomes
Retrospective (uncontrolled) study using a restrictive diet in fructose/fructans ⁹	IBS (<i>n</i> = 62) with fructose malabsorption	74% demonstrated a positive response to all abdominal symptoms over a median duration of 14 months. Adherence rate of 77%.
Randomized, double-blinded, quadruple-arm, placebo-controlled, re-challenge trial. Subjects re-challenged with escalating doses of fructans, fructose, fructose/fructans mix, glucose (placebo) ¹⁰	IBS (<i>n</i> = 25) with fructose malabsorption who previously responded to low FODMAP diet	Symptoms score significantly higher in fructose, fructose/fructans mix compared with glucose. Dose-dependent relationship
Randomized controlled, single-blinded, crossover interventional trial. Participants received high and low FODMAP diets for 2 days with 7-day washout period ¹¹	IBS (<i>n</i> = 15) and Controls (<i>n</i> = 15)	Higher levels of breath hydrogen produced on high FODMAP diet. Gastrointestinal symptoms and lethargy significantly induced by high FODMAP diet in patients with IBS.
Non-randomized study comparing low FODMAP diet with standard dietary advice ¹²	IBS (low FODMAP, <i>n</i> = 39, and standard advice, <i>n</i> = 39)	Gastrointestinal symptom scores significantly lower in low FODMAP group
Randomized controlled trial comparing habitual diet with a low FODMAP diet over 4 weeks. Diets not blinded to participants ¹³	IBS (<i>n</i> = 41)	Reduction in overall symptoms in intervention (low FODMAP) group with significantly more patients reporting adequate control compared with the habitual diet.
Randomized controlled, single-blinded, crossover trial. Participants allocated to low FODMAP diet or typical Australian diet for 3 weeks, with subsequent crossover ¹⁴	IBS (<i>n</i> = 28) and Controls (<i>n</i> = 8)	Global gastrointestinal symptoms almost halved and individual symptoms (bloating, abdominal pain, passage of wind and dissatisfaction with stool consistency) significantly reduced in IBS patients on the low FODMAP diet while no significant change reported among controls.

placebo in improving symptoms scores, global assessment or abdominal pain.¹⁸ A meta-analysis pooled data from 12 trials with a total of 591 patients with IBS, trials compared fibre (ispaghula, bran or 'concentrated' fibre of unspecified type) with placebo or a low-fibre diet in one trial.¹⁹ A beneficial effect was seen when ispaghula was evaluated in six trials, with a number needed to treat of six compared with placebo. It should be noted that when only five of the studies were included in the analysis (scoring 4 or more on the Jadad scale), the effect only reached marginal statistical significance. It has been suggested that the discrepancy between reviews exists due to a

difference in end points used; the meta-analysis used a combined end point for both global IBS symptoms and abdominal pain while in contrast the Cochrane review analysed them independently.²⁰

A more recent randomized controlled trial involving 275 patients with IBS in a primary care setting based in the Netherlands compared the effects of psyllium, bran or placebo (rice flour) over a 12-week period.²¹ Psyllium provided significantly higher response rate compared with placebo with 57% of patients achieving response (defined as >2 weeks adequate relief per month) during the first month of treatment and 59% during the second month;

however, the difference ceased being significant during the third month. Conversely, bran was only found to be more effective than placebo in the third month. There was a considerable dropout rate of 40% before completion; the highest being in those randomized to bran.

Key limitations have already been highlighted in the methodology of published studies relating to fibre supplementation in IBS including inconsistent outcome measures, challenges with adequate blinding of participants, small sample sizes, a recruitment bias of participants from secondary/tertiary care, lack of reporting of IBS subtype and pre-study dietary fibre intake.²²

Gluten

A hypothesis that gluten can cause gastrointestinal symptoms in IBS in the absence of any evidence of coeliac disease has been referred to as non-coeliac gluten sensitivity (NCGS). There is minimal evidence to support a gluten avoidance strategy in IBS.

A randomized controlled trial evaluated the use of a 4-week gluten-containing or gluten-free diet in 45 patients with diarrhoea predominant irritable bowel syndrome (IBS-D) alongside HLA-DQ2/D8 genotype analysis. A gluten-containing diet resulted in more bowel movements per day and associated with higher small bowel permeability. The effect was more marked in those who were HLA-DQ2/8 positive.²³

A double-blind, randomized, placebo-controlled, re-challenge trial using gluten was conducted for 6 weeks in 34 patients with IBS who reported prior symptom improvement on a gluten-free diet for at least 6 months.²⁴ Coeliac disease was excluded on the basis of genotyping (absence of HLA-DQ2 and HLA-DQ8) or in those that expressed the HLA-DQ2 or HLA-DQ8 haplotype by normal duodenal biopsy while on a gluten diet. All participants were negative for tissue transglutaminase and endomysial antibodies. Gastrointestinal symptoms and tiredness were significantly greater in the gluten group in comparison to placebo. There was no association with HLA-DQ haplotype.

However, a more recent randomized, double-blind, placebo-controlled, crossover trial using the

same inclusion criteria as the previous study investigated the effects of three diets (high gluten, low gluten or control with no additional protein) followed by a washout period and a 3-day re-challenge in 37 participants. Gluten-specific effects were witnessed in only 8% and were not reproduced. Moreover, a low FODMAP diet was provided for the 2-week period prior to commencing the interventional diet, and during this period, the majority of participants reported an overall improvement in gastrointestinal symptoms.²⁵

Probiotics

Probiotics are live organisms that when ingested in adequate amounts confer a health benefit to the host.²⁶ Evidence exists to suggest that probiotics may exert an effect in IBS through a number of mechanisms including attenuation of visceral hypersensitivity, altering integrity of the GI mucosa, GI dysmotility and immunomodulation. There is a growing interest in the role of intestinal microbiota in functional gastrointestinal disorders, and this topic was recently covered in detail in a Rome foundation report.²⁷

A number of systematic reviews have been published comparing probiotics to placebo in adults with IBS.^{28–32} Meta-analyses have demonstrated a modest beneficial effect on global symptoms, abdominal pain and flatulence.³³ However, studies are substantially heterogeneous with variable study designs, using different species and strains of which some appear to be more effective for particular symptoms. There is a clear need for high-quality, large trials using standard outcome measures and well-characterized probiotic preparations.

Similarly, there are limited data to support the use of prebiotics. A prebiotic is a product that when ingested encourages the growth of beneficial bacteria in the host. One double-blind, placebo-controlled trial compared a *trans*-galacto-oligosaccharide with placebo in 44 patients with IBS as confirmed by the ROME II criteria.³⁴ The prebiotic stimulated the growth of bifidobacteria and alleviated symptoms. Although promising, it is clear that further studies are required before prebiotics are recommended in clinical practice.

Lipids

Subjective surveys have indicated that many patients with IBS associate symptoms with 'fatty foods'. Patients with IBS have enhanced colonic motor activity, exaggerated rectal hypersensitivity and delayed gas transit in response to duodenal lipids.³⁵ There are little clinical data on this subject with no randomized controlled trials evaluating the role of lipid modification as an intervention in patients with IBS.

Food allergy testing

Many patients with IBS believe they suffer from a 'food allergy', and the prevalence of atopic conditions has been reported to be higher in those with IBS.³⁶ However, there is little evidence to support the role of serum food-specific immunoglobulin (Ig)E testing in IBS, and other methods such as skin prick tests have not been sufficiently evaluated.

There has been an increase in the availability of 'food intolerance' testing using serum IgG antibodies proposed to assist with exclusion diets. A few small studies have demonstrated positive results with such an approach including a 12-week trial randomized controlled diet where patients with IBS on an IgG-based exclusion diet had a significantly greater reduction in symptoms than those on a sham diet.^{37,38} However, limitations in such studies have resulted in both the European Academy of Allergy, Asthma and Immunology (EAACI) and the American Academy of Allergy, Asthma and Clinical Immunology (AAAAI) to recommend that IgG testing to foods should not be performed and may indicate a physiological response of the immune system after exposure to food rather than a food allergy. In addition, although the presence of a specific IgE antibody may indicate the potential for a reaction to occur, more frequently there is no clinical consequence to the presence of these antibodies. Well-tolerated foods should not be removed from the diet even in the presence of positive tests.^{39,40}

Conclusion

Dietary modification has shown promise as an emerging therapeutic tool in recent years. There is now

reasonable evidence to support the use of interventions such as FODMAP restriction diets and specific probiotics. A paradigm shift has resulted in a focus on the relationship between diet and pathophysiological mechanisms in IBS such as effects on intestinal microbiota, inflammation, motility, permeability and visceral hypersensitivity. Future large, randomized controlled trials with rigorous end points are required. In addition, predictors of response or development of biomarkers are required to offer personalized therapy.

Conflict of Interest statement

The authors have no potential conflicts of interest.

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