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Cover Page Footnote

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The Impacts of the Low-FODMAP Diet on the Management of Irritable Bowel Syndrome Symptoms: Possibilities, Feasibility, and Alternatives

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Irritable bowel syndrome (IBS) is a common gastrointestinal (GI) condition characterized by a myriad of GI symptoms (e.g., diarrhea, nutrient malabsorption) that vary in severity. Due to its complex and individual nature, there is no known cure for IBS, but many diets have been assessed for their viability in managing symptoms. The low-FODMAP diet has recently been investigated for its potential benefits for IBS patients. FODMAPs, or Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols are short- and medium-chain carbohydrates that are poorly absorbed in the small intestine and are prone to absorb water and ferment in the colon. Consumption of these FODMAPs correlates with increasing severity of IBS symptoms. The purpose of this randomized controlled trial systematic review was to compile various evidence-based dietary recommendations for the low-FODMAP diet for adult patients suffering from IBS from randomized controlled and clinical trials. The possibilities, feasibilities, and potential alternatives are proposed to determine if there is sufficient evidence to recommend the low-FODMAP diet for this patient population. Over 1,000 studies were screened and 6 were reviewed to determine the benefits of this diet. It was found that the low-FODMAP diet has demonstrated efficacy in delivering IBS symptom relief by changing patients' metabolomes, microbiomes, and physiology. Specifically, this diet showed a greater overall decrease in abdominal pain, bloating, stool consistency, frequency, and urgency. Greater diversity of actinobacteria was found in the stool samples of these patients. Nociceptive neurons were also shown to be less sensitive and GI gas production was also markedly decreased. Despite these benefits, the low-FODMAP diet is more recommended for acute flare-ups due to its difficult adherence and attrition. Instead, we conclude that the balanced Mediterranean diet contains aspects of the traditional Mediterranean and low-FODMAP diet that can relieve IBS symptoms for daily life, while the low-FODMAP diet can be an effective treatment to ameliorate conditions when severe symptoms are experienced.

Keywords: irritable bowel syndrome, low-FODMAP diet, IBS

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Introduction

Irritable bowel syndrome, or IBS, is a gastrointestinal medical condition that affects approximately 11.2% of the human population every year (Monsbakken et al., 2005) and is characterized by abdominal pain at an incidence rate of least once a week in the previous three months (Sood & Ford, 2016). Severity may vary, but common symptoms include abdominal pain or discomfort, typically in conjunction with diarrhea and constipation. Usually, attacks are acute, but will likely become recurrent and chronic. The causes of IBS are generally considered multi-factorial with theories ranging from changes in gut microbiota and genetics to alterations in gut motility, food sensitivity, and more (Occhipinti & Smith, 2012). Although the mechanism of action for this disease is still relatively unknown and under research, the impact on the quality of life for affected individuals is real.

Due to the variety of probable causes for IBS, treatment options may vary to cover each potential source of IBS. Since the mechanism of action is complex, a cure for IBS is probably equally complex and so the management of IBS symptoms is a more practical approach to improving the quality of life in patients. There has been evidence in the past demonstrating the potential benefits of various diets in managing IBS symptoms. Most current dietary advice for IBS involves avoiding trigger foods, modification of fiber intake, eliminating lactose, scheduling meals, and minimizing caffeine and fat consumption. These diet modifications are typically ineffective and not evidence-based recommendations (Eswaran, 2011).

A diet that has recently been under investigation for its potential uses in patients with IBS is the low-FODMAP diet. FODMAPs, or fermentable oligosaccharides, disaccharides, monosaccharides, and polyols are short-chain carbohydrates that exhibit low absorption rates throughout the small intestine and have a tendency to uptake water, while also undergoing fermentation in the colon. The consumption of FODMAPs has had correlations with increased severity of IBS symptoms potentially due to changes in osmolarity, gut microbiota, and gas production (Ong et al., 2010). Therefore, some studies have been undertaken to determine if a low FODMAP diet may relieve the severity and intensity of various IBS symptoms.

The objective of this paper is to create evidence-based dietary recommendations based on randomized controlled and clinical trials on the low-FODMAP diet for adult patients suffering from IBS. The possibilities, feasibilities, and potential alternatives are proposed to determine if there is sufficient evidence to recommend the low-FODMAP diet for this patient population.

Materials and Methods

- **1. PICO**: Does temporary use of a low FODMAP diet lower the incidence of symptoms and flares in adults with IBS (irritable bowel syndrome) compared to those, not on the FODMAP diet?
- 2. Search Strategy and Data Sources: PubMed and Google Scholar were the two different databases used throughout the month of October 2022 to search studies and articles related to the PICO question. The terms "FODMAP diet", "FODMAP", "irritable bowel syndrome", "IBS", "low FODMAP", and "low FODMAP IBS" were all used in both databases. Studies were restricted to those published recently (last 15 years), clinical trials, human trials, and written or translated into English.

3. Study Quality Assessment and Study Selection: Studies were included and selected if they met certain criteria for quality assessment. Randomized controlled trials were included if they had at least two arms of comparison. Eligible participants were adults over the age of 18. Studies were only included if they compared the effects of a low FODMAP diet to another diet or a control. The intervention in the studies had to promote an extended use of a low FODMAP diet for patients so the results could be studied. The diets that were compared to the low FODMAP in the studies ranged from a standard, control diet to different standard diet intervention types, and even higher intake of FODMAP. This was done to ensure that the low FODMAP diet can lower the incidence or severity of IBS and IBS-like symptoms in patients in comparison to various diets. Other exclusion criteria included studies that were not randomized, studies that had confounding variables, and studies that focused on children.

Figure 1



PRISMA diagram of the PICO Methodology for choosing appropriate studies.

Results

Table 1

Summary of data collected from studies selected

Article Number	Evidence Quality	Study Design	Sample size	Sex	Race/ Ethnicity	Age groups	Intervention
1	This study focused on how low-FODMAP diet can lower IBS symptoms compared to a regular diet through a randomized controlled study.	Randomized controlled trial	Total N = 78; n = 37 LFD, n = 41 ND	Male and female	All Danish Caucasian	Ages ranged 20- 70; median 40	Low FODMAP diet vs normal diet
2	The strong quality study demonstrates that the intervention has positive benefits of the low- FODMAP that largely outweigh the negatives compared to the mNICE study through a randomized controlled study.	Randomized controlled trial	Total N = 92, n = 45 low FODMAP, 39 mNICE	Male and female	Mostly non- Hispanic whites in the low FODMAP (39/50) and in the mNICE (29/39)	Median age 42.6	Low FODMAP diet vs mNICE
3	The strong quality study demonstrates that the intervention has positive benefits that largely outweigh the negatives in a low vs high-FODMAP diet.	Randomized controlled trial	Total N = 40, n = 20 low FODMAP, n = 20 high FODMAP	Male and female	N/A, study from Kingston, Ontario (Canada)	Ages ranged from 24-83 with median 50.28 and 51.47 for low FODMAP and high FODMAP respectively	Low FODMAP vs high FODMAP diets
4	The strong quality study demonstrates that the intervention has positive benefits that largely outweigh the negatives when following low-FODMAP in relation to the standard recommended diet.	Clinical Trial	Total N = 62, n = 32 BRD, n = 30 SILFD	Male and female	Thai	Ages ranged from 18 to 70 years, mean of 51 years	Commonly recommended diet (BRD) vs structural individual low-FODMAP diet (SILFD). SILFD replaces high-FODMAP with low ones. BRD involves reducing recognized food that causes IBS symptoms
5	The strong quality of this study demonstrates that the low- FODMAP has positive benefits that in comparison to various combinations of probiotic, control, and placebo diets.	Clinical Trial	Total study size of 95. 48 were in control diet, 47 were in the low-FODMAP, 45 in placebo group, 50 in the probiotic, 24 in control diet with placebo, 24 in control diet with probiotic, 21 in low-FODMAP diet with placebo, and 26 in the low-FODMAP diet with probiotic	Male and female	Mostly Caucasian from London, UK	Ages ranged from 18-65 years	Four categories were generated from a 1:1 ratio of control diet to low-FODMAP and placebo to probiotic supplement
6	The strong quality study demonstrates that the intervention has positive benefits that largely outweigh the negatives	Clinical Trial	Total N = 42, n = 28 completed all 3 diets (34 followed low-FODMAP, 30 followed gluten-free, 28 followed balanced diet)	Male and female	Italian	Ages ranged between 18 and 45 years, mean age of 28.62	Low FODMAP, followed by gluten-free, then balanced Mediterranean

Article Number	Studies aim and hypothesis	Significant Outcomes	Implications for dietetic practice	Study Reference
1	To examine how a low- FODMAP diet impacts symptoms resembling irritable bowel syndrome (IBS) in individuals diagnosed with inflammatory bowel disease (IBD).	Low Fat Diet had a statistically significant lower median IBS-Symptom Severity System (median 115) than the normal diet group (median = 170), p-value = 0.02. Additionally, the Low Fat Diet had a statistically significant elevated increase in short IBD quality of life questionnaire (median = 60) than the normal diet group (median = 50), p-value < 0.01.	This study demonstrates that a low- FODMAP diet led to significantly lower IBS symptom flares and can have benefits for individuals suffering from IBD or IBS-like symptoms.	Pedersen et al., 2017
2	To compare the effects of FODMAP vs a modified NICE diet	52% of the low FODMAP diet compared to 41% of the mNICE diet group demonstrated sufficient relief of IBS-D symptoms. The low FODMAP diet had a larger proportion of abdominal pain responders when contrasted to the mNICE diet (51% vs. 23%). Compared to the mNICE diet, the low FODMAP diet demonstrated that it had a greater reduction in mean daily score of bloating and abdominal pain. There was also an increased stool periodicity, consistency, and urgency in the low-FODMAP diet than the mNICE diet.	This study demonstrates that the low FODMAP diet may be as useful as other standard dietary interventions for patients with IBS-D symptoms	Eswaran et al., 2016
3	To gain mechanistic insights on the effects of the low FODMAP diet on symptoms, the metabolome and the microbiome of patients with IBS.	Lactulose breath tests showed a small decrease in H2 synthesis in the low-FODMAP diet compared with the high-FODMAP diet. Metabolic urine analysis demonstrated that some patients with IBS differed significantly after the diet in some metabolites. Azelaic acid, histamine, and p-hydroxybenzoic acid were primary discriminating metabolites between the two diets. Histamine, involved in immune activation, was reduced 8x in the low-FODMAP diet. Low- FODMAP diet also elevated Actinobacteria quality and heterogeneity. Meanwhile, the high FODMAP diet decreased the relative quantity of gas consuming bacteria.	IBS symptoms were associated to FODMAP food consumption and demonstrated capacity to modify the metabolome. FODMAPs were also shown to modulate immune activation through histamine levels as well as the microbiota, both of which may modify IBS- symptoms. Patients with IBS who engaged in a low FODMAP diet had improvements in symptoms and changes in their metabolome. This suggests that immune signaling and alterations in the microbiota may play an important role in symptom manifestation through mechanistic pathways in certain patients with IBS.	McIntosh et al., 2016
4	To compare the gas production in patients with IBS enrolled in a structured and individual low-FODMAP diet vs a commonly recommended diet for IBS	Total IBS symptom severity had significant improvement, while the number of high-FODMAP items consumed was significantly decreased after Structural Individual Low-FODMAP Dietary Advice (SILFD) compared to brief advice on a commonly recommended diet (BRD). Post-prandial H2 breath test after SILFD was significantly decreased when compared to post- prandial H2 test of the BRD, p < 0.001.	First RCT on low-FODMAP in Asia. This demonstrated that patients are able to make their own meals without being provided by a dietitian. Eastern and Western dietary practices vary and must also be taken into consideration when giving dietary recommendations. This advice method significantly reduced FODMAP intake, improved IBS symptoms, and lowered intestinal H2 production.	Patcharatrakul et al., 2019
5	This studied aimed to comprehensively identify gut-microbiota relationships in adult IBS patients engaging in a regular diet; analyze the impact of two distinct diet interventions on the gut microbiota; and determine whether standard, baseline gut microbiota can be used to predict potential patient responses to probiotic or diet interventions.	16S rRNA gene sequences were created for each stool sample. Low-FODMAP diet group had a 1.2% less proliferation of Bifidobacterium and 4.5% decrease in growth of unclassified Ruminococcaceae genus. The low-FODMAP group also had a 10.8% higher count of bacteria from the Bacteroides genus when contrasted with the control group. The findings of comparing the low-FODMAP diet group to the control were also supported at the family (lower Bifidobacteriaceae/ Ruminococcaceae, with higher Bacteroidaceae) and phylum level (less Actinobacteria/Firmicutes and higher Bacteroidetes).	Recommendations are limited for microbiota changes in low-FODMAP diets due to bivariate correlation. Further research needs to be performed for more robust recommendations.	Staudacher et al., 2021
6	To compare the superiority of a low-FODMAP diet over a gluten-free or balanced Mediterranean diet ⁷	Although the low-FODMAP had achieved similar results in quantitative abdominal pain relief, it was the only diet group that was able to standardize and regulate bowel function and movement. The balanced Mediterranean diet showed superior quality of life and VAS pain, due it naturally having low-FODMAPs present in the diet.	It's possible that the recommendation of a balanced Mediterranean diet might have the best options due to its adequate supply of FODMAP and is more suitable for long-term commitments.	Paduano et al., 2019

Discussion

Several studies demonstrate that the low-FODMAP diet can be used to potentially lower symptom incidence and severity in patients with irritable bowel syndrome. In general, it's been observed that participant groups on the low-FODMAP diet can help mitigate symptoms of IBS compared to control groups. The low-FODMAP diet showed a significantly lower median IBS-Symptom-Severity-Score with a median of 115 than the control group with a median of 170 (p = 0.02). Additionally, the Low-FODMAP diet group had a statistically significant larger increase in quality-of-life score with a median of 60 compared to the control's median of 50 (P < 0.01). (Pedersen, 2017).

Several of these trials have also compared the efficacy of various diets to the low-FODMAP diet, all of which have determined that the low-FODMAP is superior to others in treating patients with IBS. When contrasting the low-FODMAP diet to the traditional and standard guidelines for IBS set by the National Institute for Health and Care Excellence (NICE) guidelines, low-FODMAP showed a greater overall decrease in abdominal pain and distention, stool consistency and frequency, and urgency on a weekly and overall basis. These changes in the low-FODMAP intervention group demonstrated a greater improvement level while also having relief from abdominal symptoms in a much shorter time frame (Eswaran et al., 2016). Other clinically recommended routine dietary advice for patients with IBS was also compared to the low-FODMAP diet. The low-FODMAP diet had a significant decrease in global IBS severity (p=0.006) and H2 production (p<0.001) from baseline compared to the commonly recommended diet for IBS patients (Patcharatrakul et al., 2019).

To understand how the quantity of FODMAP consumption can affect the physiology of a patient with IBS, a study compared the symptoms, metabolome, and microbiome of patients on high and low-FODMAP diets. IBS-SSS only reduced in low-FODMAP. Minor decrease in H2 production and 3 metabolite difference (histamine, p-hydroxybenzoic acid, azelaic acid). Patients with IBS have been shown to have increased histamine in their mucosa which can lead to increased levels of mastocyte activation and primes both pain-sensing and enteric neurons. Further study must be done to understand these pathways (McIntosh et al., 2016).

FODMAPs can also function as prebiotics for certain microbial species that may play a role in IBS symptom severity and intensity. Specifically, the low-FODMAP diet demonstrated an increase in actinobacteria quality and variety, a species of bacteria thought to modulate IBS symptoms. In contrast, the high-FOM-DAP diet increased the quantity of bacteria that are involved in gas consumption, possibly potentiating IBS symptoms. The high bacterial diversity indicates that there may be multiple pathways that could lead to IBS symptoms including signaling from active or inert metabolites due to fermentation and degradation of FODMAPs by various bacteria (McIntosh et al., 2016). The microbiome of stool samples in patients with IBS was also studied and determined through a 16S rRNA gene sequencing that low-FODMAP diets produced a lower abundance of Bifidobacterium and Ruminococcacae. It also had a higher abundance of Bacteroid genus (Staudacher et al., 2021).

These studies have also been conducted in different countries in Europe, Asia, and North America achieving similar success rates in these different demographic populations. None had any significant difference in the initial symptom severity baselines between trial groups. It is important to note that despite no change in baseline, the adoption of a low-FODMAP diet presents unique challenges depending on the cultural basis of food consumption. Eastern patients tend to have high vegetable and legume consumption

which may increase the FODMAP intake of these patients (Patcharatrakul et al., 2019).

Despite the low-FODMAP's benefits for patients with IBS, it still has its limitations. First, it can be an expensive diet to maintain for patients who are not enrolled in a clinical trial. Patients might also not entirely understand which foods would fall in the low-FODMAP diet classification or misidentify the FODMAP content of foods without the guidance of a registered dietitian. The low-FODMAP diet can also be an extreme diet to maintain as it restricts many of the foods people normally consume and may create an incompatible change in lifestyle for most people. Multiple studies have reported the difficulty of following this diet (Patcharatrakul et al., 2019). To find an alternative, an Italian study determined that following a modified balanced Mediterranean diet can provide many of the same benefits of a low-FODMAP diet without compromising food selection. Although the balanced diet's effects are less profound, they can still help mitigate abdominal pain, bloating, and disease severity to improve the patient's quality of life. This indicates that following a low-FODMAP diet acutely when there is a severe flare-up of symptoms, followed by a long-term adaptation to the balanced Mediterranean may provide the best results for patients with IBS (Paduano et al., 2019). There was also data demonstrating that people's normal dietary habits tend to follow the consumption of high FODMAP foods all in one meal, leading to an increase in high-severity symptom flares in IBS. Following the Balanced Diet or a low-FODMAP diet helps disperse FODMAP consumption in meals throughout the day which can mitigate symptoms as well.

Some limitations of this study include the potential to overgeneralize the evidence-based nutritional recommendations. The studies selected were chosen from different parts of the world to allow for more general recommendations that can be applied to various populations. However, following the low-FODM-AP or Balanced Diet might not be feasible due to the differences in dietary customs and cultures, access to resources, genetics, and gut microbiota between global populations. Still, these recommendations can be helpful for those populations that are able to include the changes in their lifestyle. Although there have been many studies finding dietary associations with IBS symptoms, future work needs to be done in clinical trials toward different and more specific populations to see how demographic differences can be influenced by these same diets. Future work for this paper includes finding more targeted studies to create more definite recommendations for patients.

Conclusion

The low-FODMAP diet has demonstrated efficacy in delivering IBS symptom relief for acute flare-ups by changing patients' metabolome, microbiome, and physiology. The balanced Mediterranean diet contains aspects of the Mediterranean diet that can relieve IBS symptoms for more chronic and less severe symptoms, without the difficult conditions of the low-FODMAP diet.

Evidence-Based Nutritional Recommendation

• The low-FODMAP diet has demonstrated the potential to help alleviate IBS and symptoms similar to IBS, including abdominal pain and distention, gas production, and stool consistency while im-

proving quality of life.

- The low-FODMAP diet has the potential to change both the metabolome and microbiome of the patient in positive ways.
- Following this diet with the guidance of an RDN or other trained clinicians has demonstrated better results.
- The low-FODMAP diet can be expensive and restrictive to maintain so is recommended for short-term utilization during more severe symptom flare-ups.
 - The Balanced Mediterranean Diet can be recommended for more long-term symptom relief due to its less restrictive nature.

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