Clinical Scenario: A 26-year-old female presents to clinic with constant bloating and abdominal discomfort after meals as well as constipation, and states she was diagnosed with IBS when she was a child. With all the hype seen recently about "Gluten-Free" diets, she looked into a diet that may be better for her symptoms and came across the low FODMAP diet. She wonders if adopting a low FODMAP diet and trying to remove certain triggers from her diet such gluten, would help these symptoms resolve.

Search Question: Does the elimination of gluten and having a low FODMAP diet improve the symptoms of irritable bowel syndrome?

PICO search terms:

Ρ	1	C	0
Irritable bowel	Gluten free diet	Control diet	Overall symptom
syndrome			relief
IBS	Low FODMAP diet	Usual diet (what they	Symptom
		typically eat)	improvement
		High FODMAP diet	Reduced abdominal
			pain
		Non-restricted diet	Reduced bloating
			Constipation relief

Search tools and strategy used:

Please indicate what data bases/tools you used, provide a list of the terms you searched together in each tool, and how many articles were returned using those terms and filters. Explain how you narrow your choices to the few selected articles.

PubMed:

- Diet and Irritable bowel syndrome (Best Match) 1,504
- Diet and Irritable bowel syndrome (Best Match, Publication Date: 10 years) 1,003
- Diet and Irritable bowel syndrome (Best Match, Publication Date: 5 years) 655
- Diet and Irritable bowel syndrome (Best Match, Publication Date: 5 years, Free Full Text) 315
- Diet and Irritable bowel syndrome (Best Match, Publication Date: 5 years, Free Full Text, Meta-Analysis) – 8

Cochrane:

- Diet and Irritable bowel syndrome 2 Cochrane Reviews
- Low FODMAP diet and IBS 0 Cochrane Reviews

Google Scholar:

- Diet and Irritable bowel syndrome- 93,100
- Diet and Irritable bowel syndrome since 2016–24,700
- FODMAP diet and Irritable bowel syndrome since 2016–16,100

I selected 4 high level evidence articles that addressed my topic from the yielded results when I filtered out systematic reviews/meta- analysis.

Articles Chosen:

Citation:

Dionne J, Ford AC, Yuan Y, et al. A Systematic Review and Meta-Analysis Evaluating the Efficacy of a Gluten-Free Diet and a Low FODMAPs Diet in Treating Symptoms of Irritable Bowel Syndrome. *Am J Gastroenterol.* 2018;113(9):1290-1300. doi:10.1038/s41395-018-0195-4

Type of article:

Systematic Review and Meta-Analysis

Abstract:

Objective: Dietary triggers such as gluten and highly fermentable oligo-, di- and monosaccharides and polyols (FODMAP)-containing foods have been associated with worsening irritable bowel syndrome (IBS) symptoms. However, the true impact of dietary restriction on IBS symptoms has remained unclear. The aim of this study was to conduct a systematic review and meta-analysis of randomized controlled trials (RCTs) examining the efficacy of exclusion diets (we focused on low FODMAP and gluten-free diets (GFD)) in IBS. Methods: We conducted a search of the literature using the electronic databases MEDLINE (1946 to November 2017), EMBASE (1974 to November 2017), Cochrane Central Register of Controlled Trials (November 2017), and Cochrane Database of Systematic Reviews (2005 to November, 2017) for RCTs of exclusion diets in IBS. Two independent reviewers screened citations and a third reviewer resolved disagreement. Two independent reviewers performed eligibility assessment and data abstraction. For inclusion, RCTs that evaluated an exclusion diet versus an alternative or usual diet and assessed improvement in either global IBS symptoms or abdominal pain were required. Data were synthesized as relative risk of symptoms remaining using a random effects model. Quality of evidence was assessed using GRADE methodology.

Results: A total of 1726 citations were identified. After full-text screening a total of nine studies were eligible for the systematic review. There were two RCTs of a GFD, involving 111 participants. Both selected patients who responded to a GFD and then randomized them to continue the diet or have the diet "spiked" with gluten. A GFD was associated with reduced global symptoms compared with a control diet (RR = 0.42; 95% CI 0.11 to 1.55; I₂ = 88%), although this was not statistically significant. There were seven RCTs comparing a low FODMAP diet with various control interventions in 397 participants. A low FODMAP diet was associated with reduced global symptoms compared with control interventions (RR = 0.69; 95% CI 0.54 to 0.88; I₂ = 25%). The three RCTS that compared low FODMAP diet with rigorous control diets had the least heterogeneity between studies, but also the least magnitude of effect. The overall quality of the data was "very low" according to GRADE criteria.

Conclusions: There is insufficient evidence to recommend a GFD to reduce IBS symptoms. There is very low quality evidence that a low FODMAP diet is effective in reducing symptoms in IBS patients.

Hyperlink: http://eprints.whiterose.ac.uk/134755/1/IBS_diet_v4.pdf

Citation:

Altobelli E, Del Negro V, Angeletti PM, Latella G. Low-FODMAP Diet Improves Irritable Bowel Syndrome Symptoms: A Meta-Analysis. *Nutrients*. 2017;9(9):940. Published 2017 Aug 26. doi:10.3390/nu9090940

Type of article: Meta-Analysis

Abstract:

Irritable bowel syndrome (IBS) affects 7-15% of the general population. A recently devised dietary approach consists of restricting foods with highly fermentable oligo-, di-, and monosaccharides, and polyols (FODMAPs), which can trigger and/or exacerbate IBS symptoms. The aim of this study is to use meta-analysis to provide an update on the randomised control trials (RCTs) and cohort studies, and examine them separately in relation to diet type. Papers were selected using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart. Cohen's d and odds ratios were used as a measure of effect size for RCTs. A random effects model was used to account for different sources of variation among studies. Heterogeneity was assessed using Q statistics, P, Tau, and Tau². Publication bias was analysed and represented by a funnel plot, and funnel plot symmetry was assessed with Egger's test. The results showed that in the RCTs, the patients receiving a low-FODMAP diet experienced a statistically significant pain and bloating reduction compared with those receiving a traditional diet; as regards to stool consistency, there was no significant difference between treatments. A significant reduction in abdominal pain and bloating were described by patients receiving a low-FODMAP diet compared with those receiving a high-FODMAP diet. In cohort studies, pain and bloating were significantly reduced after treatment compared with the baseline diet. We conclude that there is evidence that a low-FODMAP diet could have a favourable impact on IBS symptoms, especially abdominal pain and bloating. However, it remains to be demonstrated whether a low-FODMAP diet is superior to conventional IBS diets, especially in the long term. Hyperlink: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5622700/

Citation:

Su H, Li YT, Heitkemper MM, Zia J. Effects of Low-FODMAPS Diet on Irritable Bowel Syndrome Symptoms and Gut Microbiome. *Gastroenterol Nurs*. 2019;42(2):150-158. doi:10.1097/SGA.0000000000000428

Type of article:

Systematic Review

Abstract:

Patients with irritable bowel syndrome (IBS) suffer from abdominal pain, bloating, and abnormal defecation. Reducing the dietary intake of fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) has been shown to be beneficial in reducing IBS symptoms. However, diet modification plays an important role in the composition of colonic microbiota. Currently, the effects of a FODMAP diet on the composition of the gut microbiome are not known. We conducted a systematic review to determine (1) the effectiveness of low-FODMAPs diet to reduce symptoms of patients with IBS and (2) the association between a low-FOMAPs diet and the composition of gut microbiome. Four electronic databases were searched using key words "IBS" or "irritable bowel syndrome," and "FODMAP" or "FODMAPs" or "fermentable oligosaccharides, disaccharides, monosaccharides, and polyols," and "microbiome." Two reviewers (H.S. and Y.T.L.) selected and reviewed articles according to our inclusion criteria. A total of 87 articles were reviewed and 7 met inclusion criteria. Based on the systematic review, low FODMAPs appear to reduce gastrointestinal symptoms for at least a subset of patients with IBS. However, due to the heterogeneity of reviewed studies, the influence on patients' gut microbiome composition and/or microbiota metabolites requires additional studies.

Hyperlink:

https://journals.lww.com/gastroenterologynursing/FullText/2019/03000/Effects_of_Low_FOD MAPS_Diet_on_Irritable_Bowel.5.aspx?casa_token=VfNRAUaYy8oAAAAA:iUHE0xpyWcdEL hecN_F8_mHm3aFg3-

HaG6geSt8_E6J3_PkotbLavUZBNNDFBDxtGEUq9u8odL02kuiUXEPRPIII

Citation:

Varjú P, Farkas N, Hegyi P, et al. Low fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) diet improves symptoms in adults suffering from irritable bowel syndrome (IBS) compared to standard IBS diet: A meta-analysis of clinical studies. *PLoS One*. 2017;12(8):e0182942. Published 2017 Aug 14.

doi:10.1371/journal.pone.0182942

Type of article:

Meta-Analysis

Abstract:

Background: Irritable bowel syndrome (IBS) and functional digestive tract disorders, e.g. functional bloating, carbohydrate maldigestion and intolerances, are very common disorders frequently causing significant symptoms that challenge health care systems. A low Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols (FODMAP) diet is one of the possible therapeutic approaches for decreasing abdominal symptoms and improving quality of life.

Objectives: We aimed to meta-analyze data on the therapeutic effect of a low-FODMAP diet on symptoms of IBS and quality of life and compare its effectiveness to a regular, standard IBS diet with high FODMAP content, using a common scoring system, the IBS Symptom Severity Score (IBS-SSS).

Methods: A systematic literature search was conducted in PubMed, EMBASE and the Cochrane Library as well as in the references in a recent meta-analysis. Adult patients diagnosed with IBS according to the Rome II, Rome III, Rome IV or NICE criteria were included in the analysis.

Statistical methods: Mean differences with 95% confidence intervals were calculated from studies that contained means, standard deviation (SD) or mean differences and SD of differences and p-values. A random effect model was used because of the heterogeneity (Q test (χ 2) and I2 indicator). A p-value of less than 0.05 was chosen to indicate a significant difference.

Results: The literature search yielded 902 publications, but only 10 were eligible for our meta-analysis. Both regular and low-FODMAP diets proved to be effective in IBS, but post-diet IBS-SSS values were significantly lower (p = 0.002) in the low-FODMAP group. The low-FODMAP diet showed a correlation with the improvement of general symptoms (by IBS-SSS) in patients with IBS.

Conclusions: This meta-analysis provides high-grade evidence of an improved general symptom score among patients with irritable bowel syndrome who have maintained a low-FODMAP diet compared to those on a traditional IBS diet, therefore showing its superiority to regular IBS dietary therapy. These data suggest that a low-FODMAP diet with dietitian control can be a candidate for first-line therapeutic modality in IBS. Because of a lack of data, well-planned randomized controlled studies are needed to ascertain the correlation between improvement of separate key IBS symptoms and the effect of a low-FODMAP diet.

Hyperlink: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0182942

Summary of the Evidence:

Author (Date)	Level of Evidence	Sample/Setting (# of subjects/	Outcome(s) studied	Key Findings	Limitations and Biases
		definition etc.)			
Dionne J, Ford AC, Yuan Y, Chey WD, Lacy BE, Saito YA, Quigley EMM, Moayyedi P (2018)	Systematic Review and Meta- Analysis	- Total of 9 studies - 2 evaluated a GF diet with 111 participants - 7 RCTs compared low FODMAP diet with various control interventions in 397 participants	- Primary outcome was global improvement in IBS symptoms - If that was unavailable, abdominal pain was the outcome of interest	 Of the 2 RCTs evaluating GFD, both trials reported a statistically significant result, but when the two trials were pooled the results were not statistically significant due to marked heterogeneity between individual trial results A low FODMAP diet was associated with a reduction in global symptoms 	- Most studies were unclear or high risk of bias, there was heterogeneity between study designs, and there was imprecision in the estimate of effect - There was variation in the comparator diet between trials
Altobelli E, Del Negro V, Angeletti PM, Latella G (2017)	Meta- Analysis	- 6 RCTs and 6 Cohort studies were included - Total: 590 participants - Three RCTs compared the traditional IBS diet to the Iow- FODMAP diet and three compared the Iow- and high- FODMAP diets - The cohort studies compared patients' conditions at baseline and after administration of the Iow- FODMAP diet	- Abdominal pain and bloating were assessed in all study types included. - Stool consistency and frequency were evaluated in all RCTs comparing FODMAP and traditional diets, so they were also included.	compared with controls. - The patients receiving a low- FODMAP diet experienced a statistically significant pain reduction compared to those receiving a traditional diet and compared to those receiving a high-FODMAP diet . - Patients managed with a low-FODMAP diet experienced significant bloating reduction compared with those receiving a	 The first limitation of this study lies in the relatively small number of primary studies. A second limitation is the lack of blinding. A third limitation is the inadequate treatment duration, which does not allow for a long-term assessment. A fourth limitation is the fact that, in the studies analysed in this meta- analysis, the FODMAP diet is never compared

				traditional diet and compared to those receiving a high-FODMAP diet. There was no significant heterogeneity. - Pain after treatment was significantly reduced compared with baseline in the cohort studies' patients. - Significantly reduced bloating was reported by the cohort studies' patients after treatment.	with the current standard dietary advice for IBS, as reported by the British National Institute for Health and Care Excellence (NICE).
Su H, Li YT, Heitkemper MM, Zia J (2019)	Systematic Review	- 7 RCTs (3 are single-blinded and 4 were double-blinded) - Total of 320 participants	 Irritable Bowel Syndrome Severity Scoring System [IBS- SSS], Irritable Bowel Syndrome Quality of Life questionnaire [IBS-QOL], GI symptoms, abdominal pain, microbiome, metabolic product, stool Consistency * Irritable Bowel Syndrome Severity Scoring System [IBS-SSS] consists of five questions that measure abdominal pain severity, abdominal pain severity, abdominal pain frequency, abdominal pain 	 All seven studies found that the low- FODMAPs diet reduced IBS symptoms (i.e. abdominal pain and stool consistency) Seven studies showed that the low-FOMAPs diet changes the microbiota composition, such as decreasing butyrate- producing bacteria, prebiotic bacteria, and mucus- associated bacterium, after low-FODMAPs diet. 	 The meal preparation in the different countries where studies were conducted could have influenced the outcomes The primary outcome measure varied across studies. These studies provided information on daily FODMAP intake, rather than the FODMAPs intake per meal, which may have a stronger relationship with symptoms.

			analogue scale (VAS)		
Varjú P, Farkas N, Hegyi P, et al (2017)	Meta- Analysis	- 10 articles - The number of controlled trials was 7, and there were 3 non-controlled prospective studies. - Of the controlled trials, 5 were randomized controlled trials (RCT), and 2 were non- randomized studies.	- IBS-Symptom Severity Score (IBS-SSS) was the main outcome parameter measured	- When comparing the pre- and post- intervention scores between the control and low-FODMAP groups in the controlled trials, there was no statistically significant difference in pre- values between the groups, but a significant difference between post- values could be observed.	 By using the complex IBS- SSS as the main outcome, it was not clear which of the five elements play a key role in the improvement of IBS symptom severity toward better personalization of this dietary approach. Because of the lack of data in the different IBS subtypes, it is not clear which subgroup experienced the greatest symptom improvement The standard IBS diet group was not homogeneous The precise content of the foods used was only detailed in 2 trials and the others probably followed dietary guidelines. This uncertainty could have influenced our results.

Conclusion(s):

Article 1: Dionne et al concluded that there was insufficient evidence to recommend a GFD to reduce IBS symptoms and that there is very low quality evidence that a low FODMAP diet is effective in reducing symptoms in IBS patients.

Article 2: Altobelli et al concluded that there is evidence that a low-FODMAP diet can have a favorable impact on IBS symptoms, especially abdominal pain, bloating, and diarrhea. However, it is still not proven whether a low-FODMAP diet is superior to conventional IBS diets, especially in the long term.

Article 3: Su et al concluded that low FODMAPs appear to be helpful in reducing GI symptoms for at least a subset of patients with IBS and that a low-FODMAP diet could be recommended to patients with IBS.

Article 4: Varjú et al concluded that a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) significantly improves general symptoms and quality of life in patients with irritable bowel syndrome.

In overall conclusion, it appears that a low FODMAP diet appears to reduce IBS symptoms.

Clinical Bottom Line:

Weight of the evidence:

All 4 articles provided high level of evidence being that they were all systematic reviews and/or meta-analyses so, there were several other factors that I took into consideration when weighing the evidence of each article and is explained below.

My first article by Dionne et al weighed the most in my search because it addressed both gluten and low FODMAP for IBS, making it the most specific to my question and concerns for the patient. I also weighed it first because it is from the respected American Journal of Gastroenterology and it is from 2018.

I weighed the article by Altobelli et al second even though it was published in Switzerland because it had the largest number of participants using both RCTs and cohort studies, which are subject to less bias.

Although the article by Su et al is the most recent of all the articles, as it was published in 2019, I weight it third because it had the least number of participants. I also weighed it 3rd because its outcomes were not only focused on IBS symptoms but also gut microbiome. Although I found this aspect of the research important when it comes to the discussion of IBS, it was not directly related to my question.

Lastly, the article by Varjú et al weighed last because it only had one outcome measured, the IBS-SSS, and didn't specify which of the five elements that are part of this scoring system played a key role in the improvement of IBS symptom severity toward better personalization of this dietary approach.

Magnitude of any effects:

Dionne et al found that a gluten free diet was associated with reduced global symptoms compared with a control diet (RR 0.42; 95% CI 0.11 to 1.55. I2 = 88%), although this was not statistically significant. There were seven RCTs comparing a low FODMAP diet with various control interventions in 397 participants. A low FODMAP diet was associated with reduced global symptoms compared with control interventions (RR 0.69; 95% CI 0.54 to 0.88. I2 = 25%). The three RCTS that compared low FODMAP diet with rigorous control diets had the least heterogeneity between studies, but also the least magnitude of effect. Altobelli et al found that patients receiving a low-FODMAP diet experienced a statistically significant pain reduction compared to those receiving a traditional diet. The overall effect size was odds ratio (OR) = 0.44; there was no statistical heterogeneity. It also found that significantly reduced abdominal pain was described by patients receiving a low-FODMAP diet compared with those receiving a high-FODMAP diet (OR = 0.17) and there was no statistical heterogeneity. Su et al did not discuss effect size but stated that there was heterogeneity amongst the studies. Finally, Varjú et al compared the pre- and post-intervention scores between the control and low-FODMAP groups in the controlled trials and showed that there is no statistically significant difference in pre-values between the groups (DIM: control minus low-FODMAP values: -8.675 (95% CI: -40.043 -+22.693); p = 0.588), but a significant difference between post-values (DIM: +51.537 (95% Cl: +18.891 - +84.183); p = 0.002) could be observed. This confirms that the therapeutic effect of a low-FODMAP diet is better than standard dietary advice in patients with IBS.

Clinical Significance:

IBS can be hard to treat because there is no one specific treatment that is indicated or prescribed. The exact course of treatment will depend on the type and severity of the symptoms experienced. IBS negatively impacts a person's quality of life and causes a substantial burden on healthcare resources. Food is a central and constant issue for patients with IBS as up to 70% of IBS patients associate symptom onset or exacerbation with certain foods. Therefore, it is important to evaluate evidence available to assess which dietary changes are most effective for those experiencing the key IBS symptoms of abdominal pain, bloating, constipation, and/or diarrhea.

Other considerations:

Being that all 4 of these articles are systematic reviews and/or meta-analyses focusing on low FODMAP diet effectiveness for IBS, it is important to note that was some overlap in RCTs used. Additionally, not all articles recommended a low FODMAP diet as strongly as the other due to their grading of evidence found. Nonetheless, each article also agreed that more data and further studies are needed. Whether it is to make all variables uniform in RCTs in order to get more accurate results, to look more into gluten free diets, patients microbiome, stool studies, or to have a higher number of patients in the studies, or to demonstrate whether the low-FODMAP diet is superior to the traditional IBS diet following the NICE guidelines in the long term, this topic requires further investigation to better understand how to tailor diets to those in IBS. The bottom line is that from the available dietary interventions, a low FODMAP diet currently has the greatest evidence for efficacy in IBS.