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Is Maintaining a Gluten-Free Diet Effective in Decreasing Symptoms for Irritable Bowel Syndrome?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

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ABSTRACT

Objective: The objective of this selective EBM review is to determine whether or not a gluten-free diet is effective in decreasing symptoms for irritable bowel syndrome (IBS).

Study Design: Systemic review of three randomized, double-blind, placebo-controlled trials published between 2010-2016, all in the English language.

Data Sources: Data sources obtained for this review were studies published in peer reviewed journals found using PubMed Database and were selected based on outcomes measured and relevance to the objective.

Outcomes Measured: The outcomes measured were based on reduction in abdominal symptoms in IBS patients. Outcomes were measured by a series of 10 cm Visual Analog Scale (VAS). The VAS monitored symptoms with 0 representing no symptoms and 10 indicating severe clinical symptoms. Symptoms observed included abdominal pain, bloating, satisfaction with stool consistency, and overall well-being. Patients completed a questionnaire on primary outcomes and symptoms. Significance of outcomes were determined using p-value, relative benefit increase, absolute benefit increase, and numbers needed to treat.

Results: All three studies showed a significant decrease in abdominal symptoms in IBS patients following a gluten-free diet. Biesiekierski et al. found a statistically significant decrease in abdominal symptoms at the end of the 6 weeks study with patients who had the gluten-free diet compared to the gluten diet ($p=0.001$). Elli et al. study also found a significant difference in patients that had the gluten-free diet compared to the gluten diet ($p= 0.001$). Shahbazkhani et al. found reduction in abdominal symptoms with a gluten-free diet ($p< 0.001$).

Conclusions: The randomized controlled trials discussed in this review suggest that a gluten-free diet is effective in decreasing symptoms for IBS.

Keywords: irritable bowel syndrome, gluten-free diet

Introduction

Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders.^{1,2} IBS is a chronic disorder characterized by abdominal pain with association of alternating bowel movements.¹ It is diagnosed with the Rome III criteria which includes having abdominal pain with 2 of the 3 criteria: abdominal discomfort relieved with defecation, change in stool frequency, and change in stool appearance. There are three main subtypes of IBS including IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), and mixed IBS (IBS-M).

Approximately 10-15% of adults and adolescents have symptoms consistent with IBS.¹

IBS affects around 11% of the population globally.² IBS is important to address in healthcare because approximately 50% of people who experience symptoms from IBS will consult a healthcare provider.³ Approximately 50% of patients with IBS report their first symptoms before the age of 35.³ Patients over 50-years-old, often have worst quality of life.³ The estimated annual cost for IBS treatment is between 1.7 billion dollars and 10 billion dollars in direct medical costs (medications) and 20 billion dollars in indirect (absentee from work) medical costs in the United States.⁴ The exact number of healthcare visits due to IBS within the past few years are not known; however, it is estimated that between 10% and 70% of patients visit their primary care provider for IBS symptoms. IBS patients are the largest subgroup seen in gastroenterology clinics.²

The cause of IBS is not completely understood. The pathogenesis of IBS is thought to be from altered gastrointestinal motility, brain-gut interactions, bacterial overgrowth, and food sensitivity.⁵ The first line methods to treat IBS are reassurance, lifestyle modifications, and dietary modifications. Pharmacologic treatment can be used to minimize symptoms including polyethylene glycol or magnesium hydroxide for constipation, loperamide for diarrhea, and

antispasmodics.^{1,5,6} Other adjunct treatments for IBS include cognitive behavioral therapy with antidepressants like tricyclic antidepressants (TCA).^{5,6}

Currently, there are several treatment options and medications that can improve the symptoms of IBS; however, there is not one single therapy that cures all IBS symptoms. The true efficacy of having a gluten-free diet is still not highly researched. It is suggested that gluten causes intestinal injury and/or inflammation in patients with IBS. Gluten is found in three types of grains including wheat, rye, and barley. Wheat has been found to be one of the most common factors to induce gastrointestinal symptoms such as abdominal pain. Evidence suggest that targeted dietary carbohydrates exclusion can provide clinical benefit to patients with IBS. Therefore, a gluten-free diet is an alternative for relief of symptoms of IBS. A gluten-free diet has shown to be effective in treatment for IBS by decreasing irritation of the intestines. This systematic review evaluates three randomized control trials to determine if maintaining a gluten-free diet is effective in decreasing symptoms for IBS.

Objective

The objective of this selective EBM review is to determine if a gluten-free diet is effective in decreasing symptoms for irritable bowel syndrome (IBS).

Methods

Criteria used for selection of studies for this systemic evidence-based review are focused on populations, interventions, comparisons, and outcomes measured. The population studied in these articles were patients with IBS using the Rome III criteria (Table 1). The patients were greater than 16 years old without any other known gastrointestinal disease including celiac disease. The intervention was a gluten-free diet compared to a gluten diet. The treatment group received a gluten diet while the control group received a gluten-free diet. The outcomes that were

measured used patient-oriented evidence that matters including improvements of the overall symptoms of IBS such as bloating, abdominal pain, stool consistency, nausea, tiredness, and general well-being while on a gluten-free diet verses a non-gluten free diet.

Research for this systematic review was obtained from PubMed that were double-blinded, randomized controlled trails published in peer-reviewed journals. All studies were published in the English language and published within the last 15 years. Key words that were searched in these articles were “irritable bowel syndrome” and “gluten-free diet.” The articles were selected based on relevance to the clinical questions and outcomes of the studies that mattered to the patients for this systematic review. The inclusion criteria were adults greater than 16 years old diagnosed with IBS that fulfilled the Rome III criteria (Table 1). The exclusion criteria were patients who have celiac disease, wheaten allergy, inflammatory bowel disease, and/or with significant gastrointestinal disease (Table 1). The summary of statistics used by these studies analyzed the data using p-value, numbers needed to treat (NNT), relative benefit increase (RBI), and absolute benefit increase (ABI) (Table 2).

Table 1: Demographics and characteristics of included studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Biesi- kierski ⁷ (2011)	Double- blind RCT	39	>16 years old	-Age > 16 years old -Symptoms of IBS fulfilling Rome III criteria -Adherence of the diet for at least 6 weeks	Patients with celiac disease, gastrointestinal disease, excess alcohol intake or intake of non- steroidal anti- inflammatory agents	5	Placebo or gluten diet, in the form of 2 bread slices plus one muffin per day for 6 weeks, both groups were a gluten free diet
Elli ⁸ (2016)	Double- blinded RCT	101	> 18 years old	-Age >18 years old -Routinely attending the gastroenter- ological clinic -Symptoms consistent with Rome III criteria	Patients with celiac disease, wheaten allergy, inflammatory bowel diseases, psychiatric disorders, major abdominal surgery, diabetes mellitus, systemic autoimmune diseases, having gluten-free diet regimen in the past 6 months, pregnant or breast-feeding women, or already on pharmacological therapy	3	Gluten free diet, placebo or gluten ingestion
Shahb- azkha- ni ⁹ (2015)	Double- blinded RCT	148	> 16 years old	-Age > 16 years old -Newly diagnosed IBS based on Rome III criteria	Patients with celiac disease, have tried a gluten free diet, on a gluten free diet, self- exclusion of wheat, inflammatory bowel disease and diabetes, using any drugs for depression and/or anxiety, used non- steroidal anti- inflammatory drugs, with abnormal lab levels	76	Placebo group (gluten-free powder) vs. gluten containing group for 6 weeks, both groups were on a gluten-free diet

Outcomes Measured

The outcomes measured in these studies were the improvements of the overall symptoms of IBS while on a gluten-free diet versus a non-gluten free diet. Outcomes collected were patient-oriented evidence that matters (POEM). Outcomes were measured using the 10 cm Visual Analog Scale (VAS). In all studies patients completed a questionnaire, patients were told to rank their symptoms on a 0 to 10 scale with 0 representing no symptoms and 10 representing the most severe. Biesikierski et al. measured the outcomes of improvement in symptoms of IBS including bloating, abdominal pain, stool consistency, nausea, and tiredness. Elli et al. measured the outcomes by satisfaction of patient's health status and the severity of symptoms including abdominal pain, satisfaction with stool consistency, bloating, postprandial fullness and general well-being. Shahbazkhani et al. measured the outcomes of improvements in symptoms of IBS including bloating, satisfaction with stool defecation, nausea, fatigue, and overall symptoms.

Results

Three randomized, double-blind trials were selected for this systemic review to determine the efficacy of a gluten-free diet for treatment of IBS. All three studies, Biesikierski, Elli, and Shahbazkhani et al. study, utilized dichotomous data based on intention-to-treat analysis. The analysis of measured outcomes for each study is based on the overall improvement of symptoms for IBS.

Biesikierski et al. study, used gluten-free diets as the placebo for the control group (n=15) versus gluten diet as the intervention groups (n=19).⁷ Changes in symptoms in patients with IBS were assessed. This study included patients greater than 16 years old, symptoms of IBS, and adherence of diet for at least 6 weeks. This study excluded patients with celiac disease, gastrointestinal disease, and excess alcohol intake. Based on the inclusion and exclusion criteria,

39 patients were included, and 34 patients were able to complete the study with 5 patients who had withdrawn from the study (Table 1). Patients that ceased the study prematurely stopped due to intolerable increase in abdominal symptoms. The patients that participated in the study received either gluten or placebo in the form of two bread slices plus one muffin per day with a gluten-free diet for up to 6 weeks. Food diaries from the patients were maintained in week 3 and week 6 of the treatment period. Adherence was measured by food supplements consumption and maintaining a gluten-free diet. Consumption was 95% and 96% in placebo and gluten groups, respectively. Patients were asked if at the end of each week if symptoms were adequately controlled. More patients in the gluten group reported “no” to symptoms well-controlled compared to the placebo group ($p= 0.001$) (Table 2). After week 1 therapy, changes in symptoms from baseline scored on the VAS were significantly different in those who had the gluten diet. The overall results of the study indicated that patients in the gluten group had a greater score in severity of pain, bloating, satisfaction with stool consistency, and tiredness. Based on the results in the Biesikierski et al. study, relative benefit increase (RBI) was -41.1%, absolute benefit increase (ABI) was -28%, and the numbers needed to treat (NNT) was -3 (Table 2). The negative ABI indicates that there was 28% increase of an adverse event as a result of the gluten diet. The negative NNT value means that for every 3 participants who had a gluten containing diet, there was one fewer incidence of decreased IBS symptoms than in the group of participants in the placebo group.

Table 2: Comparison and statistical significance of outcomes measured of included studies

Study	P-Value	RBI	ABI	NNT
Biesikierski⁷	0.001	-41.1%	-28%	-3
Elli⁸	0.001	-67.2%	-50.6%	-1
Shahbazkhani⁹	<0.001	-69.3%	-58.1%	-1

In the Elli et al. study, 140 patients were enrolled, and 134 patients completed the 3-week gluten-free diet during the first period of the study.⁸ Out of the 134 patients, 101 patients responded to a gluten-free diet and 3 patients refused randomization. In phase 2, 98 patients were randomized for either administration of placebo or gluten with a 7-day crossover. Inclusion criteria included patients greater than 16 years old and newly diagnosed with IBS based on Rome III criteria. Exclusion of patients with celiac disease, wheaten allergy, inflammatory bowel disease, psychiatric disorder, and any major comorbidities due to wanting to focus on a population group primarily with IBS. In phase 2 of the study, patients were divided into a control group (n=48) and an interventional group (n=58) where they were administered gluten supplements. Both groups were administered 7 gastrosoluble capsules per day. Each patient was administered 5.6 g of gluten content to consume. During phase 1, no adverse events were noted during the three-week gluten free diet course; however, during phase 2, one adverse event occurred during the placebo administration. Mild periorbital edema was recorded. The patients were also asked to report their general wellbeing using the VAS. The double-blind placebo-controlled challenge (DBPCC) positive indicated symptoms when eating a gluten-diet and DBPCC negative indicated no symptoms when eating a gluten-diet (Table 3). Abdominal pain was 5.4 ± 2.4 for DBPCC positive and 3.2 ± 2.8 for DBPCC negative.⁸ Based on the results the RBI was -67.2%, ABI was -50.6%, and the NNT was -1 (Table 2). The negative ABI indicates

that there was 50.6% increase of an adverse event as a result of the gluten diet. This negative NNT value indicates that for every 1 participant who had a gluten containing diet, there was one fewer incidence of decreased IBS symptoms than in the group of participants in the placebo group. The p-value is 0.001 which is statistically significant.

Table 3: Double-blind placebo-controlled challenge abdominal symptoms mean and standard deviation

Variable	DBPCC Positive	DBPCC Negative	P-value
Abdominal pain	5.4 ± 2.4	3.2 ± 2.8	0.006
Stool consistency satisfaction	4.5 ± 2.9	5.7 ± 3.0	0.08
Bloating	8.2 ± 2.8	3.6 ± 2.9	0.0001
Postprandial fullness	6.6 ± 3.0	4.9 ± 2.9	0.01
Early satiety	6.4 ± 2.8	4.4 ± 2.9	0.03
Epigastric pain	2.3 ± 2.3	3.0 ± 3.0	0.27
Other gastrointestinal symptoms	4.6 ± 4.0	3.4 ± 3.0	0.41

In Shahbazkhani et al. study, 148 patients fulfilled the Rome III criteria and were enrolled in the study between 2011 and 2013.⁹ However, only 72 patients met the inclusion and exclusion criteria and continued with the study (Table 1). Patients included were greater than 18 years old and had symptoms consistent with IBS. The patients were randomly allocated into two groups: a placebo group (n=37) that received gluten-free supplements and the interventional group (n=35) that received gluten supplements. The experimental group that received gluten were given a packet of 100 grams containing gluten meal. The placebo group received gluten-free powder in the form of packets with 100 grams containing powder of gluten-free foods. Both groups consumed the powder for 6 weeks while on a gluten-free diet. Powder packets were to be poured in a cup of water containing 150 mL of warm water, consumed at breakfast and at dinner. Weekly follow-up assessment was used to evaluate compliance of gluten-containing diet.

Optimal dietary compliance was indicated if consumption of gluten was less than 100 mg/day and those patients (8/80) that did not comply with this policy did not continue with the study.⁹ In this trial, there were no adverse events except discomfort or abdominal pain. After the 6 weeks, the patients in the placebo (the gluten-free) group had more controlled abdominal symptoms than the gluten-containing group ($p < 0.001$).⁹ There was a change in abdominal symptoms by week 1 listed in Table 4. The change in symptoms score was increased from 3.1 ± 2.3 to 5.1 ± 2.2 after having a gluten diet and was decreased from 8.4 ± 1.5 to 3.1 ± 2.3 while on a gluten-free diet (Table 4).⁹ There was also an increase in all symptoms in the gluten-containing group, most significantly in bloating and overall symptoms (Table 5). Based on the results in the Shahbazkhani et al. study, RBI was -69.3%, ABI was -58.1%, and the NNT was -1. The negative NNT value means that for every 1 participant who had a gluten containing diet, there was one fewer incidence of decreased IBS symptoms than in the group of participants in the placebo group. Therefore, having a gluten diet had more symptoms than a patient with a gluten-free diet. The p-value was <0.001 is statistically significant.

Table 4: Mean and standard deviation at week 1

Type of Treatment	Before Use (Mean \pm SD)	After Use (Mean \pm SD)
Gluten	3.1 ± 2.3	5.1 ± 2.2
Gluten-free	8.4 ± 1.5	3.1 ± 2.3

SD= Standard Deviation

Table 5: Abdominal symptoms with gluten diet vs non-gluten diet

Study Group	Symptoms				
	Overall symptoms	Satisfaction with stool consistency	Tiredness	Nausea	Bloating
Gluten-group	74.3%	77.1%	60%	8.3%	74.3%
Placebo (Gluten-free)	16.2%	8.1%	8.8%	5.4%	16.2%

Discussion

This systematic review compares three randomized, double-blind, placebo controlled clinical trials. All three studies, found improvement or reduction in IBS symptoms when having a gluten-free diet.

Gluten-free diets are used for treatment in not only IBS patients, but also in celiac patients, other gastrointestinal issues, and personal preference in diet. The availability to maintain a gluten-free diet is manageable in the United States. Unfortunately, maintaining a gluten-free diet is not convenient for every patient especially in other countries that have limited availability to gluten free products. There are no contraindications to maintaining a gluten-free diet; however, adherence is difficult. Patients would have to avoid all foods containing wheat, rye, and barley. Patients would also have to avoid hydrolyzed vegetable protein or texturized vegetable protein due to having fillers with gluten components. Having a gluten-free diet can lead to deficiencies in fiber and other nutrients. Supplements may be suggested by a provider to decrease any nutritional deficiencies.

The studies that were discussed in this systematic review contained their own limitations. In Biesikierski et al., the study population was limited by a small final number (n=34) for sample size. Recruitment of patients were difficult due to the exclusion criteria of celiac disease. It is also questionable whether patients that had improvements from the gluten-free diet were undiagnosed patients with celiac disease. The first line treatment for celiac disease patients are avoidance of gluten; therefore, those patients would have improvements in symptoms with a non-gluten diet. There is the possibility that a celiac patient was included in the data. Elli et al. study limitations included focusing on non-celiac gluten sensitivity (NCGS) patients oppose to strictly IBS patients, even though the criteria were focused on Rome III criteria. Another

weakness in the Elli et al. study is determining if the gluten dosage was high enough to activate a response in the patient. Besides limitations and weaknesses found in these studies, there were also some limitations in researching studies due to most gluten-free diet studies focused on celiac disease or NCGS instead of IBS relating to gluten-free diets.

Conclusion

Based on these three randomized, double-blind, placebo controlled clinical trials gluten-free diet is effective in decreasing symptoms for IBS. All three randomized trials, found a statistically significant improvement in symptoms of IBS including abdominal pain, bloating, stool defecation, fatigue, and overall symptoms using a gluten-free diet. These studies suggest incorporating a gluten-free diet in patients with IBS along with other current therapies could be beneficial in diminishing abdominal symptoms.

Even though with this convincing evidence, additional research should be performed to determine if efficacy in gluten-free diets have more effect on patients with IBS with constipation verses IBS with diarrhea verses IBS mixed. Additional research can also test monotherapy of gluten-free diet compared to dual therapy of gluten-free diet with pharmaceutical therapies to determine if efficacy is increased with monotherapy verses dual therapy. Lastly, additional research could determine long-term effects and benefits of having a gluten-free diet.

References

1. Anastasi JK, Capilli B, Chang M. Managing irritable bowel syndrome. *Am J of Nursing*. 2013; 113 (7): 42-52.
2. Canavan C, West J, Card T. The epidemiology of irritable bowel syndrome. *Clin Epidemiol*. 2014. 6: 71-80.
3. Corseti M, Whorwell P. The global impact of IBS: time to think about IBS-specific models of care. *Therap Adv Gastroenterol*. 2017; 10 (9): 727-736.
4. Hullisz D. The burden of illness of irritable bowel syndrome: current challenges and hopes for the future. *J Manag Care Pharm*. 2004; 10 (4): 299-309.
5. Saha L. Irritable bowel syndrome: pathogenesis, diagnosis, treatment, and evidence-based medicine. *World J Gastroenterol*. 2012; 20 (22): 6759-6773.
6. Ford AC. Treatment of irritable bowel syndrome: beyond fiber and antispasmodic agents. *Therap Adv Gastroenterol*. 2011; 4 (2): 115-127
7. Biesiekierski JR, Newnham ED, Irving PM, et al. Gluten causes of gastrointestinal symptoms in subjects without celiac disease: a double blind randomized placebo-controlled trial. *The American Journal of Gastroenterology*. 2010; 106: 508-514.
8. Elli L, Carolina T, Branchi D, Roncoroni L, Lombardo V, Bardella MT. Evidence for the presence of non-celiac gluten sensitivity in patients with functional gastrointestinal symptoms: results from a multicenter randomized double-blind placebo-controlled gluten challenge. *Nutrients*. 2016; 8 (2): 84.
9. Shahbazkhani B, Sadeghi A, Malekzadeh R, Khatavi F, Etemadi M, Kalantri E, et al. Non-celiac gluten sensitivity has narrowed the spectrum of irritable bowel syndrome: a double-blind randomized placebo-controlled trial. *Nutrients*. 2015; 7 (6): 4542-4554.