Consumption of a Low Fermentable Oligo-, Di-, Mono-saccharides, and Polyols Diet and Irritable Bowel Syndrome: A Systematic Review

Abstract
Consumption of low dietary fermentable carbohydrates, including fermentable oligo-, di-, mono-saccharides, and polyols (FODMAP) has been hypothesized to improve symptoms of irritable bowel syndrome (IBS). This study was done to summarize findings from earlier evidence on the effect of a low FODMAP diet (LFD) on the symptoms of IBS. We searched in ISI Web of Knowledge, PubMed, Scopus, and Google Scholar using the following keywords: “FODMAP” OR “oligosaccharides” OR “disaccharides” OR “Monosaccharides” in combination with “irritable bowel syndrome” or “IBS” or “Gastrointestinal Disease.” The reference lists of the relevant papers were also examined to avoid missing any publication. No time and language restrictions were applied. The relevant studies were selected through an independent search by two investigators. Overall, 778 relevant articles were found in our initial search. After reviewing title and abstracts, 763 papers were excluded from this review and 15 studies were included. All published studies were interventional studies in which patients with IBS had been recommended or randomized to receive a LFD. Three studies had quasi-experimental design, 9 were parallel randomized clinical trial and 3 studies were of randomized cross-over trials. These studies were conducted between 2009 and 2016. Nine studies were done in Europe, 2 in US, 3 in Australia, and one in Asia. Sample sizes of these studies were varied from 12 to 182. All studies had been conducted on both sexes, with the majority of participants as women (>70%). The age range was between 11 and 74 years in different studies. One study was performed on children, 9 on adults, and 5 others were in young-to-middle age groups. Duration of intervention was varied from 2 days to 16 months (2 studies with <1 week, and others with more than 2 weeks). Eight studies had suggested a significant effect of LFD on the improvement of all IBS symptoms, and 1 study had reported improvement in all symptoms except for constipation. One study had not found a significant difference between LFD and lactobacillus GG on IBS symptoms. Another paper had reported no significant effect of an LFD on IBS compared with the traditional IBS diet. The other paper had reported LFD improved 75% of diarrhea. Adherence to an LFD was not associated with the severity of symptoms. It is concluded that consumption of an LFD might reduce symptoms of IBS; however, further studies are required to shed light on inconsistencies in this field.

Keywords: Diet, fermentable oligo-, di-, and mono-saccharides and polyols, irritable bowel syndrome, review

Introduction
Irritable bowel syndrome (IBS) is a chronic debilitating functional gastrointestinal (GI) disorder,[1] in which abdominal pain is associated with defecation or change in bowel habit.[2] Common IBS symptoms include abdominal pain, bloating, constipation, and/or diarrhea.[3] It is estimated that 10%–15% of the US population[3] and 10.9% of Iranian population[4] are affected. The condition is highly prevalent among women than men. IBS is associated with a significant decrease in the quality of life[5-7] and poses a great economic burden on patients, health-care systems, and the community. It is also associated with decreased work productivity.[8,9]

Management of IBS involves reducing its symptoms. Along with the use of several medications and psychological therapy, other methods including elimination of gluten and lactose[2] from the diet and inclusion of probiotics have been suggested.[2] Some experts have suggested the use of low fermentable oligo-, di-, and mono-saccharides and polyols (FODMAP) diets for patients with IBS to alleviate their symptoms. FODMAPs are short-chain...
carbohydrates[2] which are poorly absorbed in the small intestine,[3] are highly fermentable, increasing the osmotic load in the intestine. They are widely distributed in several foods including fruits and vegetables, wheat, beans, and rye.

Few studies have examined the impact of FODMAPs on IBS symptoms. Some investigators have shown that adherence to low-FODMAP diet (LFD) has been resulted in a lower frequency of IBS symptoms.[10,11] Some others believe that the effects are sustained for short-terms and further studies are needed to examine their long-term impacts.[12,13] Given the controversies in the field, this study was therefore done to systematically review the efficacy of LFD on improving IBS symptoms.

Methods

Search strategy

We searched in ISI Web of Knowledge, PubMed, Scopus, and Google Scholar using the following keywords: “FODMAP” OR “oligosaccharides” OR “disaccharides” OR “Monosaccharaides” in combination with “Irritable Bowel Syndrome” or “IBS” or “GI Disease.” In PubMed, we searched keywords through (tiab) and (MeSH) tags. The reference lists of the relevant papers were also examined to avoid missing any published data. No time and language restrictions were applied. The relevant studies were selected through an independent search by two investigators.

Inclusion criteria

Two investigators independently, selected the articles through mentioned search strategy. Publications that conducted on humans and examined the relationship or the effect of LFDs on IBS symptoms were included in the current review.

Exclusion criteria

We excluded letters, comments, reviews, meta-analyses, ecological studies, and animal studies from this review. In total, 778 articles were found in our initial search. After screening titles and abstracts of articles, 763 articles were excluded. These publications were excluded because of the following reasons: (1) those that did not report any estimates for the association between adherence to LFD and outcomes; (2) studies that had not evaluated IBS and had considered other GI disorders, and (3) studies that had investigated a single food containing low FODMAP rather than the whole dietary intakes of FODMAPs. After these exclusions, 15 papers remained for the systematic review.

Data extraction

From each eligible study, the following information was extracted: First author, year of publication, study design, country, age range, gender, number of cases, duration of intervention, outcome, type of intervention, and study findings along with the effect sizes given for this part.

Results

In total, 778 articles were found in our initial search. After screening for titles and abstracts, 763 articles were excluded. Finally, the review was carried out on 15 articles [Table 1]. All published studies were interventional studies, in which patients with IBS had been recommended or randomized to receive a LFD. Three studies had quasi-experimental design,[11,14,15] 9 were parallel randomized clinical trials,[16,17,18,20,24] and 3 studies were randomized crossover trials.[10,12,13] These studies were conducted between 2009 and 2016. Nine studies were done in Europe,[14,16,17,18,20,22-24] 2 in US,[12,15] 3 in Australia,[10,11,13] and one in Asia.[21] Sample sizes of these studies were varied from 12 to 182. Only two studies had fewer than 30 people[12,24] and two studies had more than 100 participants.[17,20] other studies had participants between 30 and 100.[10,13,16,18,23] All studies had been conducted on both sexes, with the majority of participants as women (>70%). The age range was between 11 and 74 years in different studies. One study was performed on children,[12] 9 on adults,[11,15,18,24] and 5 others on young-to-middle age groups.[10,13,14,16,17] Duration of intervention was varied from 2 days to 16 months (2 studies with <1 week,[12,13] and others with more than 2 weeks[10,11,14-17,18-24]).

The intervention in 13 studies was LFD. One study used fructose-reduced diet[20] and the other one had used low-FODMAP rye bread.[22] The control diet was the participants’ usual diet in nine studies.[11,14-19,23,24] Some studies had enrolled IBS patients, but their control diet was Australian diet,[13] high-FODMAP diet (HFD),[11,21] regular rye bread,[22] and Typical American Childhood diet.[12] One study had compared the effects of two diets, including LFD, Normal Danish/Western diet with Lactobacillus rhamnosus GG.[17]

In all studies, the outcome variable was IBS and its symptoms such as abdominal discomfort, nausea, diarrhea, and constipation. Three studies had assessed IBS severity as outcome[14,16,17].

In terms of findings, eight studies had suggested a significant effect of LFD on the improvement of all IBS symptoms.[10,11,13,20,24] 2 studies had reported improvement in all symptoms except for constipation.[18] One study had not found a significant difference between LFD and lactobacillus GG on IBS symptoms.[17] Another study had reported no significant difference between an LFD and the traditional IBS diet.[16] One study had reported that consumption of LFD improved 75% of diarrhea. Decreased abdominal pain frequency,[12] reduced GI gas accumulations,[22] and modulation of fecal fermentation[21] was also reported following consumption of an LFD. Adherence to LFD was not associated with the severity of symptoms.

Discussion

In this systemic review, we found that most studies had reported a significant effect of LFD on IBS symptoms[10,11]
Table 1: Summary of earlier studies investigating the effect of low fermentable oligo-, di-, mono-saccharides, and polyols diet on irritable bowel syndrome included in the review

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Study design</th>
<th>Country</th>
<th>Mean age (range)</th>
<th>Gender</th>
<th>n</th>
<th>Duration of intervention</th>
<th>Outcome</th>
<th>Type of intervention</th>
<th>LFD provided?</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gisela Ringstorm et al., 2009</td>
<td>Randomized controlled trial</td>
<td>Sweden</td>
<td>26-56</td>
<td>Female/male</td>
<td>12</td>
<td>12 months</td>
<td>Gastrointestinal symptoms</td>
<td>Education on LFD</td>
<td>No</td>
<td>An IBS school improves gastrointestinal symptoms. Dietary FODMAPs induce prolonged hydrogen production in the intestine that is greater in IBS and induce gastrointestinal and systemic symptoms experienced by patients with IBS. An LFD was more effective than standard dietary advice for symptom control in IBS.</td>
</tr>
<tr>
<td>Ong et al., 2010</td>
<td>Randomized controlled crossover trial</td>
<td>Australia</td>
<td>23 (22-68)</td>
<td>Female/male</td>
<td>30</td>
<td>2 days</td>
<td>Gastrointestinal symptoms</td>
<td>LFD</td>
<td>YES</td>
<td>Dietary FODMAPs induce prolonged hydrogen production in the intestine that is greater in IBS and induce gastrointestinal and systemic symptoms experienced by patients with IBS.</td>
</tr>
<tr>
<td>Staudacher et al., 2011</td>
<td>Parallel nonrandomized trial</td>
<td>UK</td>
<td>38.1</td>
<td>Female/male</td>
<td>82</td>
<td>6 months</td>
<td>Bloating, abdominal pain, flatulence, diarrhea, constipation, nausea</td>
<td>LFD</td>
<td>No</td>
<td>The intervention was effective in managing IBS symptoms.</td>
</tr>
<tr>
<td>Staudacher et al., 2012</td>
<td>Randomized controlled trial</td>
<td>UK</td>
<td>18-65</td>
<td>Female/male</td>
<td>35</td>
<td>4 weeks</td>
<td>Bloating, abdominal pain, flatulence, diarrhea, constipation, nausea</td>
<td>LFD</td>
<td>No</td>
<td>The intervention was effective in managing IBS symptoms.</td>
</tr>
<tr>
<td>Berg et al., 2013</td>
<td>Randomized clinical trial</td>
<td>Norway</td>
<td>43</td>
<td>Female/male</td>
<td>182</td>
<td>4 weeks</td>
<td>Abdominal pain/discomfort, bloating, stool frequency</td>
<td>Fructose-reduced diet</td>
<td>No</td>
<td>Fructose-reduced diet improves symptom scores in IBS patients independent of results from the fructose breath test. LFD was effective in controlling IBS symptoms.</td>
</tr>
<tr>
<td>De Roest et al., 2013</td>
<td>Quasi-experimental</td>
<td>New Zealand</td>
<td>47</td>
<td>Female/male</td>
<td>90</td>
<td>15.7 months</td>
<td>Abdominal pain, bloating, constipation, diarrhea, nausea</td>
<td>LFD</td>
<td>No</td>
<td>Both LFD and LGG are efficacious in patients with IBS. The LFD might help the IBS patients to control and lower their IBS symptom severity scoring.</td>
</tr>
<tr>
<td>Pedersen et al., 2014</td>
<td>Randomized controlled trial</td>
<td>Denmark</td>
<td>37 (18-74)</td>
<td>Female/male</td>
<td>123</td>
<td>6 weeks</td>
<td>IBS severity score</td>
<td>LFD</td>
<td>No</td>
<td>Both LFD and LGG are efficacious in patients with IBS. The LFD might help the IBS patients to control and lower their IBS symptom severity scoring.</td>
</tr>
<tr>
<td>Pedersen et al., 2014</td>
<td>Quasi-experimental</td>
<td>Denmark</td>
<td>18-74</td>
<td>Female/male</td>
<td>19</td>
<td>12 weeks</td>
<td>IBS severity score</td>
<td>LFD</td>
<td>No</td>
<td>Both LFD and LGG are efficacious in patients with IBS. The LFD might help the IBS patients to control and lower their IBS symptom severity scoring.</td>
</tr>
<tr>
<td>Halms 2014</td>
<td>Randomized controlled crossover trial</td>
<td>Australia</td>
<td>23-60</td>
<td>Female/male</td>
<td>38</td>
<td>21 days</td>
<td>Gastrointestinal symptoms</td>
<td>LFD and typical Australian diet</td>
<td>Yes</td>
<td>The LFD improves gastrointestinal symptoms scores.</td>
</tr>
</tbody>
</table>

Contd...
**Table 1: Contd...**

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Study design</th>
<th>Country</th>
<th>Mean age (range)</th>
<th>Gender</th>
<th>n</th>
<th>Duration of intervention</th>
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<th>LFD provided?</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yoon et al., 2015</td>
<td>Randomized double-blind clinical trial</td>
<td>Korea</td>
<td>60</td>
<td>Female/male</td>
<td>84</td>
<td>14 days</td>
<td>Diarrhea</td>
<td>Low, Moderate, and HFD</td>
<td>Yes</td>
<td>The LFD improved 75% of diarrhea</td>
</tr>
<tr>
<td>Lopez et al., 2015</td>
<td>Quasi-experimental controlled crossover trial</td>
<td>Mexico</td>
<td>46.48</td>
<td>Female/male</td>
<td>31</td>
<td>21 days</td>
<td>Pain score, bloating score, flatulence score, Bristol scale result, satisfaction</td>
<td>LFD</td>
<td>No</td>
<td>LFD improved the scores for pain, bloating, flatulence, and increased the predict Bristol Scale result</td>
</tr>
<tr>
<td>Chumptazi et al., 2015</td>
<td>Randomized controlled crossover trial</td>
<td>USA</td>
<td>11.5</td>
<td>Female/male</td>
<td>33</td>
<td>5 days</td>
<td>Abdominal pain episode</td>
<td>LFD and TACD</td>
<td>Yes</td>
<td>In childhood IBS, a LFD decreased abdominal pain frequency</td>
</tr>
<tr>
<td>Bohnl et al., 2015</td>
<td>Randomized clinical trial</td>
<td>Sweden</td>
<td>18-70</td>
<td>Female/male</td>
<td>75</td>
<td>4 weeks</td>
<td>IBS symptoms and IBS severity score</td>
<td>LFD as well as traditional advise</td>
<td>No</td>
<td>A diet in low FODMAPs as well as traditional IBS dietary advice reduced IBS symptoms</td>
</tr>
<tr>
<td>Laatikainen et al., 2016</td>
<td>Randomized clinical trial</td>
<td>Finland</td>
<td>42.9 (21-64)</td>
<td>Female/male</td>
<td>87</td>
<td>8 weeks</td>
<td>Flatulence, diarrhea, constipation, abdominal pain</td>
<td>Low-FODMAP rye bread</td>
<td>Yes</td>
<td>Low-FODMAP rye bread helps IBS patients to control their symptoms and reduces gastrointestinal gas accumulation</td>
</tr>
<tr>
<td>Valeur et al., 2016</td>
<td>Randomized clinical trial</td>
<td>Norway</td>
<td>&gt;18</td>
<td>Female/male</td>
<td>63</td>
<td>4 weeks</td>
<td>IBS symptoms and Fecal fermentation</td>
<td>LFD</td>
<td>No</td>
<td>A LFD may modulate fecal fermentation in patients with IBS</td>
</tr>
</tbody>
</table>

*FODMAPs have few common characteristics. They are small molecules that contain only 1–10 sugars. They are osmotically active substances in the lumen of the intestine and also they are slowly absorbed in the small intestine. Hence, they are present in small intestine for a longtime and might increase the intestinal luminal water content. This would result in the long-time exposure of these components to luminal bacteria, which can in turn rapidly ferment these components. The result of this fermentation is the production of short-chain fatty acids and gases such as hydrogen, carbon dioxide, and in some people methane. These products can in turn led to the distention and abdominal pain, which is the main symptom in IBS patients; however, all FODMAPs do not exacerbate abdominal symptoms in patients with IBS. The severity of symptoms depends on the degree of malabsorption.*

There are two main mechanisms through which FODMAPs might accelerate the symptoms of IBS. First, in the small intestine and colon, FODMAPs can exert an osmotic effect through their malabsorption. This would in turn result in the high content of water in the colon. Some studies have shown that the intestinal output, and the osmotic load were increased by the consumption of HFDs. The abnormal accumulation of fluid in the small intestine in IBS patients following ingestion of unabsorbed carbohydrates such as FODMAPs might stimulate the symptoms in IBS patients in comparison with healthy people. However, some investigators believe that the concept that FODMAPs affect IBS symptoms related to the degree of malabsorption is not entirely correct. It was recently shown that FODMAPs elicit symptom production through visceral hypersensitivity. In addition, some FODMAPs, for example, oligosaccharides are malabsorbed in everyone due to the lack of hydrolases. FODMAPs are also rapidly fermented by colonic microflora. The increase in gas distends the bowel. This
can cause sensation of bloating and abdominal pain or discomfort. It might in turn cause increased forward movement (peristalsis) leading to diarrhea; however, in some people, it might cause constipation. Reduction in the production of breath hydrogen, which reflects the amount of gas produced by the colonic microflora, has been shown in both healthy and IBS people with a LFD.[2]

It must be kept in mind that most studies about the effects of FODMAPs restriction on IBS have been done in Western countries, and limited data are available in this regard in developing countries, where the pattern of IBS might be different from those in developed nations. On the other hand, most studies that have been done in this area are clinical trials with a small sample sizes. Because clinical trials are conducted in a short period, in which a high dose of intervention is going to be done, results cannot be easily generalized to normal life of people. Therefore, it seems that large-scale studies are required to shed light on this issue. It must also be considered conducting dietary interventions in a controlled manner is very difficult due to probable change in usual dietary intakes of study participants. In addition, blindness which is an important point in clinical trials is impossible in dietary interventions.

Another point is lack of considering all variables in these studies. Some variables such as the use of or change in the use of medications, probiotic intake, and overall dietary habits and intakes (e.g., meal frequency, caffeine, and alcohol) that might contribute to the changes in IBS symptoms have not been taken into account in some of these studies, making their interpretation very difficult. Given that, food cultures vary within different countries, so it is likely that, usual FODMAP intake of different countries varies from each other because of different foods they eat, which should be considered in interpreting the results. Because Iranian diet has high-FODMAP content; therefore, research in this area seems to be necessary in countries with high-FODMAP content.

Conclusions
The previous studies have demonstrated the efficacy of short-term use of LFD in controlling IBS symptoms; however, further data regarding the long-term effects of the diet are needed.

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Conflicts of interest
HP and AE declared no potential personal or financial conflicts of interest.

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