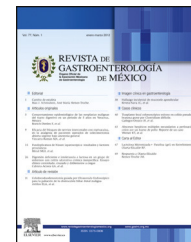




REVISTA DE  
GASTROENTEROLOGÍA  
DE MÉXICO

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## EDITORIAL

# Does a low FODMAP diet improve symptoms in Mexican patients with IBS? ☆,☆☆



## ¿Una dieta baja en FODMAP mejora los síntomas en pacientes mexicanos con SII?

Despite the fact that the majority of patients with irritable bowel syndrome (IBS) complain that foods trigger or exacerbate their symptoms,<sup>1</sup> the role of diet in IBS has not been adequately studied. It is very common for IBS patients to experiment with changes in their diet or limit the intake of certain foods, even before seeking medical attention.<sup>2</sup> The most frequently implicated foods are wheat, corn, dairy products, coffee, tea, and citrus fruits. Therefore, it is not surprising that in a study of more than 1,200 patients with IBS, 63% were interested in knowing which foods to avoid. In fact, in relation to lifestyle changes, the aspects patients put in first place were eating small meals, increasing fiber intake, and avoiding fats, carbohydrates, dairy products, caffeine, alcohol, and high protein foods, such as meat.<sup>3</sup> In addition, many IBS patients believe they have food allergies, even though these are actually very rare.<sup>4</sup> Nevertheless, the majority of food-related IBS symptoms appear to be triggered by food intolerance.

In the last few years, sensitivity to gluten and the fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) has become the main research objective as a dietary cause of IBS symptoms. In fact, the most recent review carried out by the American College of Gastroenterology for establishing IBS treatment recommendations published in 2014 concluded that “specialized diets can improve symptoms in individual IBS cases”. However, this recommendation was graded as weak, due to the

low level of evidence available during the 5 years prior to the review’s publication.<sup>5</sup> In the monograph summary it was stated that, albeit belatedly, studies have finally begun to analyze the role of dietary factors in IBS pathogeny. They focus mainly on 2 mechanisms, intolerance and hypersensitivity, but others, such as intestinal hormone stimulation and interaction with the microbiota, should not be ruled out. The summary ended by stating that a gluten-free and low FODMAP diet is promising, but its exact role in IBS management needs to be defined.<sup>5</sup>

In this sense, these two dietary factors are worth emphasizing. First, I will refer to the role of gluten. In an interesting review on celiac disease (CD) and non-celiac gluten sensitivity (NCGS), Aziz et al. give a historical account pointing out that human exposure to wheat began only 10,000 years ago in Southwest Asia, and its expansion lasted up to the year 4000 B.C.E.<sup>6</sup> In relation to the latter, it was in the 1940s that efforts were begun to increase the production of wheat, which was achieved at the end of the 20th century, with a 5-fold greater output. Thus wheat can be considered a “new” addition to the human diet, being a possible cause of an immunologic reaction in genetically susceptible subjects, leading to the presence of CD and NCGS in those individuals.<sup>6</sup> CD is characterized by chronic inflammation of the proximal small bowel mucosa that cicatrizes when foods containing gluten are excluded from the diet and recurs when they are reintroduced. Gluten contains storage proteins derived from wheat, barley, and rye. These proteins are rich in glutamine and proline and are partially digested in the upper gastrointestinal tract, resulting in peptides that can trigger an immunologic reaction.<sup>7</sup> The diagnosis can be made through the presence of type IgA anti-transglutaminase antibodies (tTG IgA) and is confirmed through biopsies of the small bowel. In 10% of the cases, the patients are seronegative, due to IgA deficiency. Therefore, when there are symptoms such as unexplained diarrhea and

☆ Please cite this article as: Schmulson M. ¿Una dieta baja en FODMAP mejora los síntomas en pacientes mexicanos con SII? Revista de Gastroenterología de México. 2015;80:177–179.

☆☆ See related content at DOI: <http://dx.doi.org/10.1016/j.rgmx.2015.06.008>, Pérez y López N, et al. Clinical response in Mexican patients with irritable bowel syndrome treated with a low diet low in fermentable carbohydrates (FODMAP). Revista de Gastroenterología de México. 2015;80:180–185.

iron deficiency anemia, endoscopy with small bowel biopsy should be performed. The other important diagnostic component is HLA-DQ2/DQ8, given that 100% of the patients present with these alleles. Due to their 100% sensitivity for CD, they are only useful for disease exclusion, because of their high negative predictive value.<sup>7</sup> For its part, NCGS is characterized by the presence of gastrointestinal symptoms (e.g. diarrhea, pain, subjective abdominal bloating) and/or extraintestinal symptoms (e.g. headache, fatigue, irritability, attention deficit, ataxia, mouth ulcers) triggered by foods that contain gluten in patients in whom CD or gluten allergy have been excluded. Symptoms improve or disappear when gluten is suppressed from the diet. There are no diagnostic or serologic criteria for this disorder but some studies have suggested the variable presence of IgA/IgG anti-gliadins.<sup>8</sup> NCGS has become very popular and there is an impressive number of patients with and without IBS in clinical practice that suspend gluten from the diet and report symptom improvement. The turning point was in 2011, when Biesiekierski et al. published a study in which patients with IBS, after a period on a gluten-free diet, were randomly divided into a gluten-free diet group vs a group ingesting 16 g of gluten daily.<sup>9</sup> They found a lack of adequate symptom control in 68% of the patients assigned to the gluten group vs 40% in the gluten-free diet group ( $p = 0.0001$ ). Symptoms were significantly worse with gluten for abdominal pain, subjective bloating, fatigue, satisfaction with stool consistency, and overall symptoms, but not for wind or nausea.<sup>9</sup> The same group published a new study 2 years later, considered a "correction to the previous study", that was conducted on patients with IBS according to the ROME III criteria and on NCGS patients. They underwent a low FODMAP diet for 2 weeks, resulting in significant symptom reduction.<sup>10</sup> These patients were then randomly divided into a high gluten diet (16 g/day) group vs those on a low-gluten diet (2 g/day) plus 14 g of whey protein. This was followed by a washout period and a 3-day crossover treatment. They showed that the high gluten diet, and not the low gluten diet and/or placebo, was significantly superior in relation to overall improvement, bloating, stool consistency satisfaction, and wind, as well as a trend in relation to abdominal pain. But there were no effects on tiredness and nausea.<sup>10</sup> The above indicates that the majority of patients that report sensitivity to gluten, in fact, present with an intolerance to FODMAPs, probably a product of the fructans—which are oligosaccharides (FODMAPs) present in wheat—and not to gluten as such.<sup>11</sup> This has been shown in later studies by other research groups.<sup>12</sup>

At present, there is no test for the diagnosis of intolerance to FODMAPs and perhaps only the fructose breath test can be useful in a subgroup of patients.<sup>13</sup> In clinical practice, the most useful test is probably a low FODMAP diet guided by a nutritionist and progressive food reintroduction for determining specific intolerances. Both adherence to these diets and their effectiveness is high in the majority of patients that use them. However, caution should be exercised, given that some low FODMAP diets have important probiotic effects on health. The decrease in fermentable substrates arriving at the colon can have at least theoretical implications in relation to carcinogenesis and inflammation, and the low FODMAP diet reduces a variety of important nutritional components as well.<sup>14</sup>

In Mexico, there are currently no data on the sensitivity to FODMAPs in patients with IBS. Only one national multicenter study interviewing more than 1,670 IBS patients found that 57% reported symptoms with legumes (galactans, fructans?) and 57% with dairy products (lactose) as symptom triggers, which were only behind high fat content foods (72%) and spicy or strongly seasoned foods (70%) as the most frequent. No association was found with artificial sweeteners (polyols?).<sup>15</sup> Nevertheless, it should be mentioned that in our clinical practice we see many patients with IBS that report symptoms such as bloating, flatulence, abdominal pain and/or diarrhea and that also have the custom of chewing gum. Currently, the majority of chewing gums are sweetened with sorbitol, followed by isomaltol and maltitol (polyols), and the gum-chewing patients improve simply by stopping the habit.

In this issue of the *Revista de Gastroenterología de México*, Pérez y López et al. present the first study in Mexico on IBS patients treated with a low FODMAP diet (< 0.50 g per meal) for 21 days. Thirty-one patients were included, of which 87% were women. The patients were given a list of "prohibited" foods during the treatment period. The authors found a significant reduction in pain, abdominal bloating, and flatulence evaluated through visual analogue scales. In addition, 29.0% reported complete treatment satisfaction, 25.8% moderate satisfaction, 16.1% slight satisfaction, 16% no changes, and 12.9% dissatisfaction. No changes were found in stool consistency evaluated through the Bristol Scale.<sup>16</sup>

Even though this is a first analysis in our environment, the results should be interpreted with care, given that the study has certain limitations, as do the majority of studies evaluating dietary interventions in IBS. Despite the fact that the authors describe their study as a "comparative" analysis, the most important limitation is precisely the lack of a control group that included the average or regular diet of the study population, with both diets having the same nutritional content.<sup>17</sup> In regard to dietary intervention trials, the Rome Foundation's Working Group on the Role of Foods in Functional Gastrointestinal Disorders has recently recommended as the ideal, a double-blind, controlled design that includes a food challenge. However, on the one hand, there is the difficulty of suitable masking, as is to be expected with this type of intervention, and on the other hand, there must be an adequate washout period before the food challenge is then gradually introduced.<sup>17</sup> It is also recommended to describe the presence of active treatments in both groups and the history of reactions to foods or the perception of food intolerances, adherence to the dietary intervention, and the presence of adverse events related to the study diet. There should also be a dietician in the group and the analysis should be controlled for factors that can interact with the food challenge, such as concomitant medication use, alcohol, and physical activity, among others.<sup>17</sup> None of these have been described by Pérez y López et al.<sup>16</sup>

In conclusion, even though the data in the literature suggest that the majority of patients with NCGS, in fact, present with intolerance or sensitivity to FODMAPs and that a diet low in these fermentable carbohydrates and polyols can improve IBS symptoms in the patients that use it, this diet should be administered under the supervision of an expert

nutritionist. Furthermore, the designs used in the majority of studies that have evaluated the low FODMAP diet in IBS are not adequate for arriving at a solid conclusion with respect to the effectiveness of this intervention.

### Financial disclosure

Max Schmulson has received financial support from the Research Division of the Faculty of Medicine of the *Universidad Nacional Autónoma de México*.

### Conflict of interest

In the past year, Max Schmulson has been a Speaker for Alfa Wassermann and Takeda México, as well as a Consultant for Commonwealth Laboratories Inc and Senosiain. He has also received research funding from Alfa Wassermann.

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