DOI:
10.1093/ajcn/nqab381

Document Version
Peer reviewed version

Citation for published version (APA):
Whelan, K. (2021). FODMAPs or gluten as inducers of symptoms in irritable bowel syndrome: separating the wheat from the chaff. *The American journal of clinical nutrition*, *115*(2). https://doi.org/10.1093/ajcn/nqab381

FODMAPs or gluten as inducers of symptoms in irritable bowel syndrome: separating the wheat from the chaff

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Short running head: FODMAPs and gluten in IBS

Sources of support: None

Conflict of interest: The author has received research funding from Almond Board of California, Danone, International Nut & Dried Fruit Council and is the co-inventor of a mobile app to support low FODMAP dietary management in IBS and of volatile organic compound biomarkers in the diagnosis and dietary management of IBS.

Abbreviations:

FODMAPs: Fermentable oligosaccharides, disaccharides, monosaccharides and polyols

IBS: Irritable bowel syndrome

IBS-SSS: Irritable bowel syndrome - Severity Scoring System

Keywords: FODMAPs, gluten, IBS, functional bowel disorders

Food is complex mixture of molecules some of which perform beneficial physiological functions, whilst diet and eating and drinking perform important psychosocial roles. However, in some people, gastrointestinal (patho)physiology can mean that some foods result in adverse gut symptoms, and avoidance of these foods can impair food-related quality of life.

Irritable bowel syndrome (IBS) is a chronic functional bowel disorder characterized by abdominal pain and altered bowel habit (either diarrhea, constipation or both). It is a significant problem, with a pooled global prevalence of 1.5% to 4.1% (1), and results in individual burden and impaired quality of life (2). The majority of people with IBS associate symptoms with consumption of at least one food. Self-reports of food-induced symptoms result in a wide range of culprits including onions, cabbage, fried foods, milk, grains, garlic, bread and pasta (3). Excluding all of these self-reported intolerances is not the correct approach to managing gut symptoms in IBS, not only because it can result in a highly restricted diet, but also because self-reports can be an inaccurate estimate of true response.

Firstly, people can incorrectly assign specific food components as being responsible for symptoms. Family doctors, gastroenterologists, dietitians and nutritionists may be familiar with patients reporting they cannot tolerate gluten, the protein component in the cereals wheat, barley and rye. However, gluten is never consumed in isolation and many other molecules could be potentially responsible for gut symptoms, including other components of the cereal (e.g. fructans, amylase/trypsin-inhibitors) and components of other foods routinely consumed alongside them (e.g. fructans in onions and garlic and galacto-oligosaccharides in beans often added to sauces served with wheat pasta, lactose in cheese served in wheat bread sandwiches).

Secondly, the ‘nocebo effect’ is common in IBS (4), whereby when a person consumes a food they believe they cannot tolerate, they anticipate and subsequently experience symptoms, despite the absence of a strong physiological mechanism.

In some areas of clinical practice, such as severe food allergy, and in research studies, the gold standard approach to identifying adverse reactions to food is an isolated double-blind challenge, which effectively minimizes these two problems of mixed exposure and the nocebo effect.

Nordin et al. (5) report the results of a double-blind, placebo-controlled, randomized, three-arm, cross-over trial in 110 people with IBS. Participants consumed a gluten-free diet that was low in fermentable carbohydrates (fermentable oligosaccharides, disaccharides, monosaccharides and polyols, FODMAPs) for two weeks and then received in random order blinded challenges of rice porridge supplemented with either gluten (17.3 g/d), FODMAPs (50 g/d), or placebo for one week, separated by one week washout periods. In the 103 participants who completed the study, symptom scores, measured using the validated IBS-Severity Scoring System (IBS-SSS), were higher during blind challenge with FODMAPs (mean 240) than both gluten (mean 208) and placebo (mean 198), with gluten inducing symptoms no different from placebo. These scores were driven in particular by increases in abdominal distension and frequency of abdominal pain. However, there were no differences in stool frequency or consistency or quality of life between the challenges (5).

This is not the first study to demonstrate that following a blind challenge, FODMAPs, but not gluten, result in modest gut symptoms. In a smaller study of similar design, 59 people with non-celiac gluten sensitivity, approximately one third of whom also fulfilled criteria for IBS, had higher symptoms scores during challenge with fructans (a type of FODMAP found commonly in wheat) compared with gluten or placebo, again with gluten inducing symptoms no different from placebo (6).

Furthermore, there is some mechanistic evidence in support of these observations. In a study of people with IBS who also self-reported gluten sensitivity (non-celiac gluten sensitivity), a low FODMAP diet resulted in symptom reduction together with a large reduction in syndecan-1, a marker of generalized epithelial injury, which occurred irrespective of the presence of high (16 g/d), low (2 g/d) or zero (placebo) amounts of gluten (7).

In the Nordin et al. study (7), some may question the lack of harmonization between doses of the challenges of FODMAPs (50 g/d) and gluten (17 g/d). However, the dose at which different molecules induce gut symptoms is not a constant, whilst the background dietary intake of different food components can be highly variable. Therefore, attempting to harmonize the dose of challenges, for example to 17 g/d of both FODMAPs and gluten, would actually result in the opposite occurring, as this would equate to considerably above-population intake for gluten and considerably below-population intake for FODMAPs. Therefore, in the current study harmonization of challenges was attempted through doses that both reflected approximately 1.5-fold greater than population intakes (7).

Limitations of the current study were that two participants were accidentally randomized to the wrong order of challenges and the inclusion of some people outside the inclusion criteria (e.g. for age, BMI, IBS subtype). However, both of these are openly reported, and the authors performed an analysis to show these did not impact the primary outcome.

Dietary restriction of FODMAPs (termed a low FODMAP diet) is now a widely used approach in the dietary management of IBS (8). A systematic review of 12 randomized controlled trials (9) reported a moderate impact of the low FODMAP diet on symptom reduction in IBS, including a mean reduction in IBS-SSS score of -45 points, a very similar effect size to the increased score of +42 between placebo and FODMAP challenges in the Nordin et al. study (5). Meanwhile, a recent network meta-analysis reported the low FODMAP diet was superior to standard dietary advice, sham dietary advice and habitual dietary advice for achieving improvement in global IBS symptoms (10). In contrast there is less evidence for the role of a gluten-free diet in IBS, with a systematic review identifying only two randomized controlled trials which when pooled did not result in significant numbers with symptom improvement (11).

These studies indicate that FODMAPs induce greater symptoms than gluten in people with IBS. This is of profound importance to the clinician faced with patients with IBS who avoid gluten, perhaps unnecessarily, and provides evidence to initiate conversations regarding challenging and reintroducing specific foods back into the diet. However, there are three important features to remember in this endeavor. First, this study does not show that all patients with IBS are sensitive to FODMAPs and that none are sensitive to gluten, indeed there were widely individual responses to blind challenges. Second, FODMAPs resulted in only modest symptoms, indeed the numbers reporting a clinically significant or large increase in symptoms (defined as either >50 or >100 increase in IBS-SSS score, respectively) were similar between FODMAPs, gluten and placebo. Third, gut symptoms are highly sensitive to psychological distress (12). Taken together, this supports the need for integrated management of IBS that involves a gastroenterologist, a specialist dietitian and psychologist to support patients to identify and manage food-induced gut symptoms in IBS (12).

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