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Conflicts of interest

The authors disclose no conflicts.

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Not All Effects of a Gluten-Free Diet Are Due to Removal of Gluten

Dear Sir:

How gluten might cause symptoms in the absence of celiac disease and other evidence of immune activation associated with it is a subject of intense interest. The report by Vazquez-Roque et al¹ represents a very detailed analysis of 45 gluten-ingesting patients with diarrhea-predominant irritable bowel syndrome (IBS) who were randomly placed on a gluten-containing diet (GCD) or a gluten-free diet (GFD), for which food was supplied, to determine whether there were any differences in multiple endpoints in intestinal structure and function. Indeed, differences were noted in indices related to intestinal permeability, and these seemed to be exaggerated in the patients expressing HLA-DQ2 and/or -DQ8. The conclusion of the study was that “gluten alters barrier function.” We have concerns about this statement.

The interventions comprised GFD versus GCD, not gluten versus no gluten. Alteration of the gluten content of the diet has effects on dietary constituents in addition to gluten. For example, gluten coexists with the nonabsorbed oligosaccharides, fructans, and galacto-oligosaccharides (GOS). We measured the content of fructans and GOS in a range grains and cereals.² These data have been adapted to Figure 1, where the products that are gluten-free those gluten-containing have been highlighted. For nearly all the products, there was a close association of the presence of gluten with the fructan and GOS content. The only exception is the legume family (represented by haricot beans), which is high in GOS. The menus provided by Vazquez-Roque et al indicate that legumes were not a part of the GFD offered. Hence, the GFD fed to patients would have had a much lower fructan and GOS content than the GCD.

This difference is of more than theoretical interest because fructans and GOS are major subtypes of poorly absorbed short-chain carbohydrates that we have termed FODMAPs.³ In patients with IBS, these are capable of triggering gastrointestinal symptoms and their restriction in the diet has accumulating evidence of efficacy in such patients (reviewed in Gibson et al³). The differences in change of bowel habits observed between the 2 dietary groups may well have reflected differences in FODMAP rather than gluten content. The effect of altering FODMAP intake on intestinal permeability has not been studied.

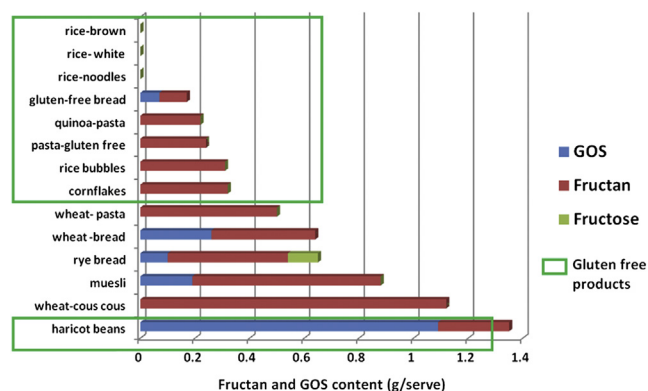


Figure 1. The fructan and galacto-oligosaccharide (GOS) content of cereals and legumes (represented by haricot beans).² The foods that are gluten free are shown within the green boxes.

The entity of nonceliac gluten sensitivity and the role of gluten as a trigger of symptoms in patients with IBS is controversial for 3 main reasons. First, separating gluten from FODMAP-induced effects has not occurred in most previous studies. Second, the only 2 studies that have reported using FODMAP-depleted gluten in randomized, controlled, blinded designs have yielded varying results according to the study design. Evidence was found for gluten being a trigger for symptoms in a parallel group study,⁴ but no evidence was detected for gluten-specific triggering of symptoms in consecutive cross-over studies on a low FODMAP dietary background.⁵ Third, a mechanism by which gluten might induce gut symptoms has been lacking. The study by Vazquez-Roque et al offers potentially important insights into this, although a gluten-specific effect was not demonstrated, as discussed.

One of the reasons the whole story of gluten and its pathogenic relationship to conditions such as IBS is so murky and controversial is that assumptions are made that response to GFD is owing to the removal of gluten. This is clearly not so with regard to symptom improvement in patients with IBS.⁵ It would be a pity if the major piece of work by Vazquez-Roque et al¹ were spoiled by inaccurate and unsubstantiated extrapolation.

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