

Optimal Testing for Diagnosis of Fructose Malabsorption: Under-dosage Leads to False Negative Intolerance Test

TO THE EDITOR: With great interest we have been following the discussion about our study published in *Journal of Neurogastroenterology and Motility*.¹ We highly estimate the recent constructive comments expressed by the authors Erdogan and colleagues² and would like to make some conclusive remarks.

We fully agree with the authors that all patients with irritable bowel syndrome (IBS)-like symptoms should undergo breath testing and have specifically stated this in our manuscript. Thus, we are not sure where Erdogan et al² got the notion that such tests should only be performed for research purposes.

We furthermore agree with Erdogan et al² that 2 consecutive breath tests are impractical, especially considering the bothersome symptoms that patients experience during and after testing. Therefore, we favor the breath test with 50 g fructose. From our yet unpublished data we know that H₂ breath tests with 50 g fructose identify patients with IBS-like symptoms who will benefit from a fructose-reduced diet. If only 25 g tests were performed, an important subgroup (the ones with symptomatic 50 g breath test) would be missed although they greatly benefit from a detailed dietary counseling, while patients with positive 25 g breath test already benefit from brief dietary advice as shown by a decline in gastrointestinal (GI) symptoms, improved quality of life and state of health. In patients with severe fructose malabsorption only the detailed dietary advice regimen resulted in improvement of GI symptoms and perceived state of health. This is our rationale to perform a breath test with 50 g of fructose.

The German consensus paper on clinically relevant breath tests in gastroenterological diagnostics does not always recommend a test with 50 g. It points out that in case of highly suspected fructose malabsorption, the high dose test should be performed first and in case of a positive outcome, an additional 25 g test enhances specificity.³

On the other hand, the rationale to start with the low dose is

that healthy volunteers almost never malabsorb 25 g. Thus, the test has an excellent specificity because, according to test criteria, there are rarely false positives. However, we feel that the low dose test lacks sensitivity because a proportion of negative low dose breath testers will still respond to a fructose elimination diet.

To deal with the lower specificity in the high dose test, observing symptoms during the test can help: increased H₂ excretion combined with typical symptoms triggered by the high dose challenge is a good criterion to distinguish between true and false positive patients, and healthy volunteers barely report symptoms even though they may have elevated H₂ excretion.⁴ Some healthy subjects and patients with IBS-like symptoms are able to fully absorb 50 g of fructose because otherwise, every test person would have significant H₂ excretion and symptoms. In our study 64% were symptomatic fructose malabsorbers with a 50 g test dose, which in reverse implies that 36% of patients with unclear abdominal discomfort were able to absorb 50 g of fructose without clinical symptoms.

We disagree with the authors that amounts > 25 g of fructose are nowadays not consumed at once. As recently outlined, a 16-oz bottle of apple juice may contain > 30 g fructose and a 22-oz soft drink could contain approximately 30 g to 40 g depending on the percent fructose in the corn syrup sweetener,^{5,6} both representing liquids regularly consumed by a large proportion of the population.

As clinicians we will accept false positives. They may undergo a 4-6 weeks dietary trial and not respond. But it is unpleasant to exclude patients, in whom most of the treatments have failed, from a fructose elimination diet that works most of the time in these patients because their diagnosis was missed. Thus, we find it more appropriate to use the high dose test with 50 g because we feel that it is clinically more relevant.

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Conflicts of interest: None.
