Every Breath Test You Take: Practical Advice on Breath Testing Used to Detect Small Intestinal Bacterial Overgrowth

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The review by Drs. Massey and Wald, published in this issue of *Digestive Diseases and Sciences* [1], is a timely reminder regarding the availability and pitfalls of the use of noninvasive breath tests for the identification of small intestinal bacterial overgrowth (SIBO) in patients with non-specific gastrointestinal symptoms. Massey and Wald have provided the evidence for their recommendation to strongly discourage performance of the lactulose hydrogen breath test due to the confounding influence of accelerated orocecal transit, including false positives manifesting as elevations of either breath hydrogen or methane. The authors identified important principles and approaches regarding the diagnosis of SIBO in Table 1 of their article. We provide here a practical format that can be used in the clinical setting or in the laboratory where the test is performed, as shown in the algorithm in Fig. 1.

In the recent past, the field of SIBO has been the subject of consensus statements, guidelines, and clinical practice updates [2–4]. Though the recommendations to use 75 g of glucose with breath sampling for 90 min coupled with the use of lower values of bacterial colony-forming units (CFU [10^3] per mL) may be acceptable for testing patients with risk factors for and/or metabolic complications consistent with SIBO, when applied to the testing of otherwise healthy individuals referred for the evaluation of nonspecific symptoms including bloating, the interpretation of such tests can be problematic. Since an estimated 16% of the US adult population experiences bloating, and the positivity rate for breath tests performed to search for SIBO is very high, when applied indiscriminately, such recommendations will likely lead to a large number of false positive tests. At our

institution, the breath test (performed under conditions more restrictive than current recommendations) has a positivity rate when glucose is used as a substrate of 23%, and with lactulose, it is 34%—similar to rates of positivity reported elsewhere for control subjects. This mirrors the number of patients with nonspecific gastrointestinal symptoms who undergo serological testing for celiac disease, which reveals only the background population prevalence of < 1%. Therefore, it is likely that the frequent positive results encountered with the breath test are unrelated to true SIBO, but simply reflect the background positivity rate of the test in the population at large.

If SIBO is truly causing bloating in otherwise healthy patients, one would expect some demonstrable underlying abnormality beyond the positive breath test. Yet, careful radiographic studies [5] and intestinal gas dynamic studies [6] have not demonstrated excessive volume or production of intestinal gas or compatible metabolic abnormalities in these patients.

Massey and Wald emphasize that the breath test has frequent false positives due to rapid orocecal transit times when used with lactulose as well as with glucose. Several studies document that to properly perform the breath test, orocecal transit times should be assessed simultaneously by scintigraphy, with breath samples obtained every 15 min for 60–120 min, which is achievable primarily in the research setting. Nonetheless, even accounting for the orocecal transit issue in this manner, the review explains that additional false positive results may arise from the discharge of endogenous mucopolysaccharides present in secreted mucus or transfer of residual ileal carbohydrates (derived from a prior meal) to the colon with subsequent metabolism and release of the gases by the normal colonic microbiome (gastroileal reflex). Moreover, severely constipated patients may liberate pre-formed hydrogen in stool in response to oral intake of even unfermentable substances (gastrocolic reflex).

When faced with a positive breath test that has a very high false positive probability, the options are: first, look

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Fig. 1 Summary of when to do a glucose breath test and how to interpret the results of the test. Adapted from Table 1 of Massey and Wald [1]

for corroborating objective evidence such as nutritional deficiency or small bowel anatomical disorders; or second, perform a reference standard test; or third, offer a therapeutic trial. In the otherwise healthy patient, there is, by definition, never any corroborating evidence. There is also no true reference standard test to offer for SIBO (1, and therapeutic antibiotic trials on the scale necessitated by the high rate of positivity would be problematic, particularly since the improvement lasts only for a median of 6 days after stopping therapy [7], requiring continuous or very frequent courses of antibiotics, with the attendant elevated harm/benefit ratio of antibiotic therapy for the treatment of such a common condition and benign as bloating in an otherwise healthy population.

Finally, though antibacterial agents, particularly rifaximin [8], may improve bloating in irritable bowel syndrome (IBS) patients, it is unclear that such a response results from actually treating SIBO since the composition of the gut microbiome does not significantly differ from that of subjects receiving placebo in non-constipated IBS [9] and further since rifaximin also accelerates colonic transit [9]. Finally, there is also evidence that rifaximin reduces

bloating scores in patients with predominant bloating and flatulence, despite a negative breath test [10].

In summary, we agree strongly with Drs. Massey and Wald that the use of the lactulose breath test should be strongly discouraged, that the use of the glucose breath test should be limited to patients who have recognized predisposing anatomical conditions or metabolic abnormalities or deficiencies consistent with true SIBO, and that performance and interpretation of the glucose breath test should be constrained by adherence to evidence-based guidelines, as shown in Fig. 1 and Table 1 of the Massey and Wald review [1]. As the implications of a positive test in the absence of predisposing anatomical conditions or nutritional deficiencies are further analyzed, the authors agree with the need for caution when basing therapy on the results of a positive glucose breath test that is not performed or interpreted appropriately.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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