SIBO in Gastroparesis: Sci-fi or Science Fact?

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Received: 18 December 2013 / Accepted: 20 December 2013 / Published online: 17 January 2014
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Gastroparesis consists of symptoms such as nausea, vomiting and abdominal pain in the presence of impaired gastric emptying and in the absence of mechanical obstruction. In addition to these hallmark symptoms, early satiety, bloating and postprandial fullness are also frequently reported and in some cases can be the prime symptoms prompting evaluation. Small intestinal bacterial overgrowth (SIBO) is defined as increased or abnormal bacteria in the proximal gastrointestinal tract. Although not all subjects with SIBO are symptomatic, those who are often report symptoms of bloating, distention and abdominal discomfort. Thus, both entities can come to clinical attention for similar symptoms, and both are often considered in the differential diagnosis of refractory non-specific gastrointestinal symptoms. Nevertheless, the relationship between these two conditions remains unclear.

The diagnosis of SIBO is clouded by lack of clear consensus regarding optimal diagnosis. The current gold standard is $\geq 10^5$ bacteria colony-forming units/mL in a jejunal aspirate, a test hampered by difficulties obtaining a sterile specimen, non-uniform distribution, the requirement for an invasive procedure (enteroscopy), lack of capability for quantitative culture by most microbiology laboratories, difficulties with cultivating most bacterial strains, and even in optimal situations, poor reproducibility [1, 2]. For these reasons, breath testing is a useful indirect measure of SIBO. Lactulose and glucose breath tests were designed with the assumption that fermentation of ingested carbohydrates by small intestinal bacteria will produce excess

hydrogen or methane in the breath. An early increase in breath concentration of these gases or an abnormal pattern of gas excretion is needed to diagnose SIBO. These tests, though often used due to their simplicity, low cost, and lack of invasion, are far from perfect. Perhaps the major problem with the interpretation of breath tests for SIBO is that their results can be significantly affected by gut motility. While elevations in hydrogen concentration within a specified time period (usually 90 min) are presumed to be due to small bacterial gas production, this early elevation of breath hydrogen concentration can also be produced by cecal bacteria if rapid transit is present. This important point was argued in a recent study by Yu et al. [3] where the authors evaluated lactulose breath tests in conjunction with simultaneous scintigraphy in patients with irritable bowel syndrome, noting that the vast majority of early hydrogen peaks were explained by variations in oro-cecal transit rather than by SIBO. The authors defined absence of SIBO only on the basis of ≥ 5 % of the test meal in the cecum at the time the lactose hydrogen breath test was positive. Nevertheless, this definition does not account for the possible association of rapid transit with SIBO in and of itself. Further, other confounding factors are present, such as false-positives due to carbohydrate malabsorption due to celiac disease or chronic pancreatitis, lactulose fermentation by oral microbiota, interference by prior fiber ingestion, recent meals, tobacco, or exercise. In addition to these factors, there are also numerous criteria that have been proposed for a positive carbohydrate breath test, further muddying the waters [4]. Due to all of these factors, there has been a wide range quoted for sensitivity (17–89 %) and specificity (44–100 %) in the literature [2, 5]. Nonetheless, sensitivity and specificity calculation are likely to have little meaning in the absence of a universally accepted gold standard. Despite these limitations, carbohydrate breath

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testing utilizing lactulose or glucose is currently the most commonly employed test to evaluate for SIBO in the United States.

In this issue of *Digestive Diseases and Sciences*, George et al. [6] evaluate the relationship between SIBO and gastroparesis. They evaluated 471 patients who underwent a lactulose breath test (LBT) and gastric scintigraphy, identifying 201 patients with delayed gastric emptying. Of that group, 79 patients (39 %) had an abnormal LBT suggestive of SIBO. Criteria for an abnormal LBT included a hydrogen concentration increase >20 ppm above baseline within 90 min, dual hydrogen peaks (>10 ppm increase over baseline prior to a second peak of >20 ppm), and an increase of methane concentration >20 ppm above baseline within 90 min. Of the 79 patients with gastroparesis and a positive LBT, 30 had a positive test by the first criterion (hydrogen rise within 90 min), 53 had a positive test by the dual peak criterion, and only six had a positive breath methane test, with little overlap among the three groups. The authors noted that in the gastroparesis patients with a positive LBT by the first criterion, there was a statistically significant increase in the severity of bloating, early satiety and postprandial fullness as compared to LBT negative patients. No statistically significant difference was seen with the other two LBT criteria.

This study is interesting for two reasons. First, the authors provide data suggesting that a sizeable subgroup of patients with gastroparesis may also have an abnormal LBT suggestive of SIBO. For the reasons detailed above, breath testing for SIBO is fraught with controversy since a positive breath test does not necessarily denote SIBO; however, the main limitation of the breath test is that positive gas production may be a manifestation of rapid transit rather than abnormal small intestinal bacteria populations. Presumably in patients with documented gastroparesis, that is not the case as—if anything—impaired gastric emptying should be associated with slower transit, with a predicted higher rate of false-negative studies. While one cannot exclude differential emptying of solids and liquids in this population (as scintigraphic gastric emptying in this study measured the rate of solid food disappearance), these data suggest that concerns regarding high false-negative rates for SIBO breath testing in patients with documented gastroparesis may be overstated [2]. That patients with an early hydrogen rise had statistically more bloating than those patients with gastroparesis supports the clinical usefulness of the LBT. The fact that impaired gastric emptying usually is associated with related motility abnormalities which may independently predispose to SIBO supports the mechanistic plausibility of this conclusion [7, 8].

The second interesting aspect of this study was the relatively little overlap between the three criteria used in this study to define a positive LBT. Because hydrogen-consumptive bacteria vary among individuals (methanogens, sulfate-reducing bacteria, acetogens), it is not surprising that few subjects simultaneously produced hydrogen and methane within the first 90 min. Despite the fact that the dual peak criterion used in this study is often considered a defining LBT pattern in support of a SIBO diagnosis [9–11], only nine patients with a dual peak pattern also had early production of >20 ppm of either hydrogen or methane. Moreover, there was no statistically significant correlation between the identification of a dual peak pattern and clinical symptom severity. In contrast, fewer patients had identification of an early hydrogen rise of >20 ppm, but those patients had a statistically significant correlation between their positive LBT and symptom severity. Since much of the controversy regarding the clinical significance of the LBT stem from the multiple interpretive criteria employed, the data from this study imply that elimination of the dual peak criterion for SIBO may add diagnostic utility to the LBT.

In view of this paper and a smaller prior study by Drs. Reddymasu and McCallum [12] it is possible that LBT, when interpreted using the early hydrogen peak criterion, may prove useful in helping define a subset of gastroparesis subjects who might benefit from a course of oral broad-spectrum antibiotics. Given the limited treatment options available for gastroparesis patients, including the lack of availability of effective prokinetic drugs in the United States, this non-invasive test may move into the mainstream in this population. This study also highlights the need for the establishment of rigorous criteria for breath testing, including creating strict guidelines for patient selection, methodology, pattern interpretation, and symptom correlation.

Conflict of interest None.

References

1. Fan X, Sellin JH. Review article: Small intestinal bacterial overgrowth, bile acid malabsorption and gluten intolerance as possible causes of chronic watery diarrhoea. *Aliment Pharmacol Ther.* 2009;29:1069–1077.
2. Quigley EM, Abu-Shanab A. Small intestinal bacterial overgrowth. *Infect Dis Clin N Am.* 2010;24:943–959.
3. Yu D, Cheeseman F, Vanner S. Combined oro-caecal scintigraphy and lactulose hydrogen breath testing demonstrate that breath testing detects oro-caecal transit, not small intestinal bacterial overgrowth in patients with IBS. *Gut.* 2011;60:334–340.
4. Lin HC. Small intestinal bacterial overgrowth: a framework for understanding irritable bowel syndrome. *JAMA.* 2004;292:852–858.

5. Khoshini R, Dai SC, Lezcano S, Pimentel M. A systematic review of diagnostic tests for small intestinal bacterial overgrowth. *Dig Dis Sci*. 2008;53:1443–1454.
6. George NS, Sankineni A, Parkman HP. Small intestinal bacterial overgrowth in gastroparesis. *Dig Dis Sci*. (Epub ahead of print). doi:[10.1007/s10620-012-2426-7](https://doi.org/10.1007/s10620-012-2426-7).
7. Bures J, Cyrany J, Kohoutova D, et al. Small intestinal bacterial overgrowth syndrome. *WJG*. 2010;16:2978–2990.
8. Bohm M, Siwec RM, Wo JM. Diagnosis and management of small intestinal bacterial overgrowth. *Nutr Clin Pract*. 2013;28:289–299.
9. Gasbarrini A, Corazza GR, Gasbarrini G, et al. Methodology and indications of H₂-breath testing in gastrointestinal diseases: the Rome Consensus Conference. *Aliment Pharmacol Thera*. 2009;29:1–49.
10. Ghoshal UC, Ghoshal U, Das K, Misra A. Utility of hydrogen breath tests in diagnosis of small intestinal bacterial overgrowth in malabsorption syndrome and its relationship with oro-cecal transit time. *Indian J Gastroenterol*. 2006;25:6–10.
11. Ghoshal UC. How to interpret hydrogen breath tests. *J Neurogastroenterol Motil*. 2011;17:312–317.
12. Reddymasu SC, McCallum RW. Small intestinal bacterial overgrowth in gastroparesis: are there any predictors? *J Clin Gastroenterol*. 2010;44:e8–e13.