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Breath Testing and Small Bowel Organisms in Clinical Practice

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STUDY HIGHLIGHTS

What is Known

- Breath testing is used to assess for small bowel bacterial overgrowth
- Antibiotics are prescribed based on breath testing
- Response to treatment is variable

What is New

- Normal microbial content of the small bowel is not clearly defined
- Breath tests can be difficult to interpret
- Diet drives microbial content of small bowel

Translational Impact

- More complete understanding of the small bowel content is required before the breath test can be understood and appropriately applied to clinical situations

The article by Peinado Fabregat et al (1) in this issue presents their observations of a retrospective review of charts from a single center on the findings of children who underwent a breath test (BT) from June 2012 to October 2018 to assess for small intestinal bacterial overgrowth (SIBO). The BTs were instituted on the orders of the prescribing physician who also made the decision about whether to use glucose or lactulose as the substrate. Their goal was to characterize symptoms and describe treatment and treatment efficacy for children who had a positive BT.

Although glucose is absorbed in the proximal small bowel, and lactulose is not absorbed by the small bowel, the sensitivity and specificity for either to diagnose SIBO is highly variable (2), thus the investigators include both in their analysis.

Assessment of the microbial content of the small bowel is difficult and invasive. Difficulty lies in the attempt to obtain a sample that is not contaminated by more proximal contents of the gastrointestinal tract and invasive because it requires intubation. Human breath offers a readily accessible, noninvasive, although indirect, window to the internal milieu that is used to diagnose SIBO among other diseases. Unfortunately, BT has poor sensitivity and specificity for diagnosing bacterial overgrowth when compared with cultures (2). The execution of BT and interpretation of the results are controversial (3), although as the authors discuss, most clinicians avoid antibiotics and proton pump inhibitors for specified times before the test and prescribe a period of fasting, as well as avoiding exercise and smoking. Instructions for patient preparation need to advise the consumption of a low fiber diet for at least the day before the study as foods containing fiber can be associated with an elevated baseline and erroneously suggest a positive test. The authors were careful to follow the recommendations but do not discuss diet. This is an important omission as one of their definitions of a positive BT was an elevated baseline. In addition, oral-cecal time varies and if this is not taken into consideration results can be mistakenly interpreted (4,5).

The normal microbial content of the small bowel is not fully unveiled. Culture has been the gold standard to which tests to assess for bacterial overgrowth have been compared. Some have defined the threshold for SIBO as greater than 10^3 CFU/mL (6). But culture is inadequate to identify many organisms and more recently sRNA analysis has been used (7). With this tool Saffouri et al (7) show that SIBO, defined as 10^5 CFU/mL, does not correlate with small intestinal microbial dysbiosis nor with symptoms; rather, some symptomatic subjects have an overabundance of bacteria found in healthy microbial communities and others who do not have SIBO demonstrate dysbiosis. Further diet drives the gut microbial community (8,9). The Saffouri study showed that 80% of those consuming a high fiber diet who where placed on a low fiber, high simple sugar diet developed symptoms that resolved with discontinuation of the intervention. Perhaps these observations explain the confusing results Peinado Fabregat et al found with respect to treatment. For example, 60.7% of their subjects experienced resolution with a probiotic. The composition of the probiotic could make a difference if the goal was to improve the composition of the microbiota. The investigators have no information on the probiotic or the gut microbiotic composition and we can only wonder how symptom resolution came about. Is it possibly explained by a placebo effect (10)? It is interesting that 30% of children treated with an antibiotic did not have resolution of symptoms and less than 20% of those continued to have a positive BT. Again, could these findings be explained by diet?

The investigators tell us about the Archaea population of the gut in some of their subjects by finding that 27 or 48% had methane in their breath. Archaea is the only organism that produces methane and does so by using H_2 and CO_2 produced by bacteria (11). The authors noted an association between constipation and methane production, as others have noted. However, some studies failed to find that association (12). Does the association suggest that Archaea is the cause of the symptoms? Is finding Archaea in the gut then SIBO? Dysbiosis? If indeed constipation is associated with Archaea, will eliminating Archaea relieve the constipation and/or the symptoms for which the BT was initiated? Or will adequate treatment of the constipation relieve the symptoms for which the BT was initiated. We cannot discern answers to these questions based on available data, nor can we understand if treating the constipation will eliminate Archaea and hence the symptoms for which the BT was performed. Indeed, were symptoms usually associated with constipation the very reason for the BT?

Fortunately, the highly interesting study raises a multitude of questions that will propel the field forward and questions that can

Received August 30, 2021;accepted October 23, 2021.
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The authors report no funding and conflicts of interest.
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JPGN Reports (2022) 3:2(e186)
ISSN: 2691-171X
DOI: 10.1097/PG9.0000000000000186

only be answered when the actual contents of the small bowel are assessed in conjunction with the BT. The most important question, despite the use of BT to diagnose SIBO, is does it actually do so? Finally, this study leads us to ask what do BTs measure with respect to SIBO and is that measurement clinically useful?

ACKNOWLEDGMENTS

R.D.B. made substantial contributions to the conception of the work and drafting/revising it critically for important intellectual content; approved the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. S.S.B. made substantial contributions to the conception of the work and drafting/revising it critically for important intellectual content; approved the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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