Dig Dis Sci (2015) 60:1120–1122
DOI 10.1007/s10620-014-3519-2

EDITORIAL

Connecting the Dots Between Gastrointestinal Motility and Symptoms Using Wireless Motility Capsule Testing

Kenneth Barshop · Braden Kuo

Published online: 11 January 2015

The overlap of symptoms experienced by subjects with visceral hypersensitivity and those with motility disorders often confounds clinical diagnosis. The ascertainment of the physiological mechanisms responsible for GI symptoms is often challenging for clinicians and investigators alike. As a result, treatment of these disorders is largely empiric, often based on patient symptoms rather than on the underlying pathophysiology.

Although slowed gastric motility is the defining feature of gastroparesis, the correlation between gastric emptying time and symptom severity is not well established [1, 2]. Such a correlation would simplify the treatment of gastroparesis since accelerating gastric motility with prokinetic agents would have a high probability of improving the cardinal symptoms of nausea, vomiting, heartburn, bloating, upper abdominal pain, and postprandial fullness. Despite no demonstrated correlation, it is evident in clinical practice that a subset of gastroparesis patients respond well to prokinetic agents, whereas others are refractory to treatment. Predicting the patient subset that is likely to respond to prokinetics would be of great clinical use, since it would reduce the number of patients unnecessarily exposed to ineffective treatments and associated adverse drug effects.

If such a biomarker correlating symptom with a measurable process is to emerge, it will be essential to segregate patients with "pure" (homogeneous) motility disorders from those with visceral hypersensitivity. Albeit an oversimplification of a heterogeneous group, this population can be thought of as on a spectrum, with pure motility disorders on one extreme, and pure sensory disorders on the other. According to the paradigm, pure prokinetic therapy would have minimal effect on symptom alleviation in patients with pure sensory dysfunction, since their symptoms are generated by visceral neural hypersensitivity, not hypomotility. On the other extreme, patients with pure motility disorders would in theory benefit from prokinetic agents since they treat the underlying pathophysiology. In actual clinical practice, most patients have mixed etiology, which impedes successful treatment. Without a biomarker correlating gastrointestinal symptoms to motility or other measures, empiric therapies are the norm.

The wireless motility capsule (WMC) is a modality used to assess multiregional gut motility in this patient population that has been increasingly used, mostly at advanced tertiary care centers. The WMC is a pill-sized device that travels throughout the gastrointestinal tract for 5 days after ingestion, continuously sampling intraluminal pH, temperature, pressure, and motility parameters. Unlike conventional antroduodenal manometry, the enhanced capabilities of the WMC support the simultaneous and convenient measurement of antroduodenal contractility and transit enabling regional or full gut assessment of motility.

In this issue of *Digestive Diseases and Sciences*, Arora et al. [3] highlight this complexity in their article "Clinical utility of wireless motility capsule in patients with suspected multiregional gastrointestinal dysmotility." They characterize their patients with suspected motility disorders using WMC testing, reporting multiregional dysmotility in nearly half of their sizable population of patients with upper and lower GI symptoms, in concordance with

K. Barshop
Pritzker School of Medicine, University of Chicago, Chicago, IL, USA

B. Kuo (✉)
Division of Gastroenterology, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114, USA
e-mail: bkuo@mgh.harvard.edu

previous studies [4–6]. Evaluating the global gut motility profile of these patients can be helpful in aiding clinicians to determine whether there is a focused or diffuse sensory or motility process leading to symptom generation, so that appropriate treatments can be instituted.

Using a retrospective chart review in which the common symptoms of upper and lower GI motility were considered as being present or absent, the authors again failed to find significant correlations between these two variables, in concordance with previous studies [7, 8]. The authors thus concluded that WMC testing is useful for characterizing multiregional dysmotility, and in distinguishing between patients with a functional disorder and those with motility disorders, also documenting that symptoms were poor predictors of the anatomical regions affected by dysmotility.

Is there truly no relationship between motility and symptom severity? No line connecting these dots of pathophysiology and presentation? We would argue that if ever a biomarker is to emerge, there is an abundance of well-conducted research to suggest it will not be using the current methodology of trying to connect the presence of binary symptoms to the relatively simple measure of transit times. A complex problem in a heterogeneous population must be analyzed using a multi-dimensional approach. Arora et al. provide further support for the existing body of evidence, and in doing so indirectly provide guidance for future research studying the relationship between gastrointestinal symptoms and motility using wireless motility capsule testing. We have proposed a summary of what clinicians and investigators currently advocate:

1. Transit times are not the answer.

The measurement of transit times is an oversimplification of complex physiological (or pathological) processes. Although transit time is easily measured using WMC testing, it ignores valuable contractile pressure data. Transit times are assessed using the pH sensor of the WMC; however, the pressure sensor provides a wealth of contractile information including contraction frequency and amplitude; these data are vast, relatively unstudied, and ripe for exploration.

2. Symptoms must be assessed through validated questionnaires.

The broad overlap of upper and lower GI symptoms in this diverse population makes a binary, yes-or-no approach less meaningful than assessing symptoms as continuous variables through validated instruments. For example, the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM) is a validated measure of symptom severity in patients with upper and lower GI disorders, providing multiple continuous measurements for the severity of symptoms such as nausea, bloating, postprandial fullness, and upper and lower GI pain. A complex motility profile requires sophisticated symptom characterization focusing on symptom severity. Furthermore, the timeframe over which a validated questionnaire assesses patient symptoms can be a key variable. For example, since PAGI-SYM assesses symptom severity over the preceding 2 weeks, a motility test performed on one day may not be representative of 2 weeks' worth of symptoms that precede it. Although using a narrower time window or averaging motility tests over time might better capture this relationship, the ideal symptom time window is not yet established in this regard.

3. Patients with pure motility disorders must be separately analyzed from those with elements of significant visceral hypersensitivity.

If a relationship exists between dysmotility and symptoms, it would be far easier to define this relationship in patients with motility-predominant dysfunction since patients with pure sensory disorders, and those with a mixed disorder will likely confound the relationship. Since defining these populations is difficult, one approach is to limit analysis of patients to those with delayed motility, such as a gastric emptying time of >5 h as assessed by wireless motility capsule. While this does not completely exclude patients with a mixed motor and sensory disorder, it eliminates the pure sensory cohort, thereby defining a population which might yield results superior to most current studies.

Although early work employing careful subject selection using these criteria has been promising [9, 10], larger, prospective studies are needed to determine if there is a connection between GI symptoms and motility.

Arora et al. further demonstrate the need for the GI motility community to better understand how existing therapies affect multiregional motility. The value of characterizing patients with multiregional dysmotility is reduced by the lack of location-specific motility agents, which in theory may be superior to drugs with global prokinetic actions, such as in the use of gastric pacemakers.

Incorporating WMC testing into trials for emerging prokinetic drugs could be extremely helpful in gaining insight into how future therapies might affect multiregional motility, with the ultimate goal of providing therapy tailored to an individual patient's pattern of dysmotility.

References

1. Tran K, Brun R, Kuo B. Evaluation of regional and whole gut motility using the wireless motility capsule: relevance in clinical practice. *Therap Adv Gastroenterol*. 2012;5:249–260.

2. Lee A, Wilding G, Kuo B. Variable abnormal physiological motility in the proximal upper gastrointestinal tract in gastroparesis. *Neurogastroenterol Motil*. 2012;24:652–657. (e276).
3. Arora Z, Parungao J, Lopez R, Heinlein C, et al. Clinical utility of wireless motility capsule in patients with suspected multiregional dysmotility. *Dig Dis Sci*. (Epub ahead of print). doi:10.1007/s10620-014-3431-9.
4. Rao SS, Kuo B, McCallum RW, et al. Investigation of colonic and whole-gut transit with wireless motility capsule and radiopaque markers in constipation. *Clin Gastroenterol Hepatol*. 2009;7:537–544.
5. Sarosiek I, Selover KH, Katz LA, et al. The assessment of regional gut transit times in healthy controls and patients with gastroparesis using wireless motility technology. *Aliment Pharmacol Ther*. 2010;31:313–322.
6. Bonapace ES, Maurer AH, Davidoff S, Krevsky B, Fisher RS, Parkman HP. Whole gut transit scintigraphy in the clinical evaluation of patients with upper and lower gastrointestinal symptoms. *Am J Gastroenterol*. 2000;95:2838–2847.
7. Locke GR, Zinsmeister AR, Fett SL, Melton LJ, Talley NJ. Overlap of gastrointestinal symptom complexes in a US community. *Neurogastroenterol Motil*. 2005;17:29–34.
8. Kuo B, Maneerattanaporn M, Lee A, et al. Generalized transit delay on wireless motility capsule testing in patients with clinical suspicion of gastroparesis, small intestinal dysmotility, or slow transit constipation. *Dig Dis Sci*. 2011;56:2928–2938.
9. Barshop K, Staller K, Semler J, Kuo B. Duodenal rather than antral motility contractile parameters correlate with symptom severity in gastroparesis patients. *Neurogastroenterol Motil*. 2014. doi:10.1111/nmo.12496.
10. Barshop K, Semler JR, Barton ME, Dukes GE, Kuo B, Barshop K. Duodenal rather than antral motility parameters correlate with symptom severity in patients with diabetic gastroparesis. *Am J Gastroenterol*. 2014;109:S101–S123.