ADVANCES IN IBS

Current Developments in the Treatment of Irritable Bowel Syndrome

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Capsule Technologies for Disorders of Gut-Brain Interaction: Hope or Hype?

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G&H What are the advantages and limitations of capsule technologies/wireless motility capsule testing?

BK Capsule technology is extremely exciting because it is an evolution in diagnostics. In the beginning, diagnostics were noninvasive but required radiology or fluoroscopy involving radiation, and then endoscopy allowed us to see the tissue of lesions directly but as an invasive procedure requiring a fixed center with anesthesia. The next evolution in diagnostics, which has aspects of the endoscope and aspects of information gleaned by imaging technology beamed wirelessly into a receiver, can be done in an ambulatory setting. Patients may start the test at the hospital but continue it at home, without being stuck to a machine or exposed to radiation, and a much longer-term result is obtained. Instead of snapshots, the test provides days of data with real-time monitoring. This is capsule technology in general. Video capsule endoscopy divorced video imaging of the luminal gastrointestinal (GI) tract away from an endoscope to a video on a capsule that is swallowed and can go to places that are not easily reachable by endoscope.

One of the fundamental challenges with motility testing is that many integral functions of GI motility take longer than 2 hours. The process of normal digestion of a solid meal takes about 4 hours. With abnormal motility, which is the reason for the test, this digestion process may take 10 to 15 hours. Monitoring a patient in an endoscopy suite over this time is impractical. An advantage of capsule technology is that it can be started in a 20-minute ambulatory visit and the data collected over 1 day or up to 8 days in real time. Being able to see fully how material is moving through the entire GI tract is quite an advancement over the measuring of pressures for short periods with invasive tubes.

A disadvantage is that typical measurement of motility is traditionally understood in terms of the patterns obtained from having multiple sensors over a fixed, defined length. This allows visualization of a pattern of movement or activity from one part of the GI tract to another, and many useful motility patterns have been described. The reality is that this is not practical on a capsule. Currently, only one pressure sensor can be placed on the capsule. Dynamic motility is measured by a single sensor, not from an array of multiple sensors. However, even that single measurement is powerful because it is over a considerable period of time and the entire length of the GI tract, rather than looking only at a segment at one particular time period.

G&H What capsule technologies for GI diseases are currently available, and what are they designed to do?

BK Two capsules have been approved by the US Food and Drug Administration (FDA) for the GI tract. The first, the video capsule, which I described, is commonly used to diagnose reasons for GI bleeding that have not been found by upper endoscopy and colonoscopy. These

include lesions in the small intestine (the approximately 23 feet that cannot be easily reached) and mucosal changes. Such diagnoses might be severe patchy celiac disease, severe patchy inflammatory bowel disease, or strictures that may be subtle. The second is the wireless motility capsule (WMC). An earlier iteration of the WMC, the SmartPill (Medtronic), was approved for measuring total gut transit, temperature, and pressure. Medtronic recently decided to sunset the manufacturing of this capsule, and that has had a significant impact on the availability of this technology. However, other companies are trying to fill the void. Recently, a study was published by our conglomerate multicenter group, which Dr William Chey and I led, to validate the Atmo Capsule (Atmo Biosciences). The Atmo Capsule is different from the SmartPill in that it measures GI transit not by pH but by hydrogen, carbon dioxide, and oxygen concentrations. Changes in gas concentrations serve as landmarks for when the capsule transitions from the stomach to the small intestine and from the small intestine to the colon. In this clinical trial, participants were asked to swallow the Atmo Capsule and SmartPill in random order, and gastric emptying time, colonic transit time, and whole gut transit time for each capsule were measured. The Atmo Capsule was demonstrated to be equivalent to the SmartPill, and it received FDA clearance in June 2025 for evaluation of motility disorders.

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G&H What is the diagnostic utility of WMC testing for evaluating patients with suspected GI transit delay?

BK Patients can present with a variety of common, nonspecific GI complaints that may involve the upper GI tract (eg, nausea, vomiting, early satiety, abdominal pain) or the lower GI tract (eg, abdominal pain, bloating, diarrhea, constipation). Typically, endoscopy and radiology are done to rule out any inflammation or blockage. However, many patients have negative findings that leave the clinician wondering what is causing their symptoms. The next step is to evaluate whether GI motility issues are contributing to the patient's symptoms. GI motility is generated by nerve interaction between the nerves and the muscles of the gut that work together to propel digestive food contents and other materials from one end of the GI tract to the other. Abnormal or deranged propulsion can cause symptoms. However, even more helpful is when patients present with GI complaints, but the WMC test shows normal gut transit. Often, a normal test result, rather than an abnormal one, is more useful because it exonerates gut transit motility in terms of the motor aspects of the neurons. Consequently, by default, the clinician can focus on the sensory aspects of the GI tract neurons as contributing to the patient's symptoms. All too often, without this objective testing, the clinician cannot tell the difference. Treating the motor aspects vs the sensory aspects, or both, requires different types of medications, so this is an important distinction. Primary GI clinicians who lack experience with WMC technology must make these diagnoses empirically, which can be difficult for them—and the patient. Having this type of objective information is important in terms of the diagnostic decision tree and makes everybody feel more comfortable about which way they should be headed.

G&H Which patients with disorders of gut-brain interaction are likely to benefit the most from WMC testing?

BK In a patient with a disorder of gut-brain interaction, the brain is interacting with the gut neurons, which then mediate both gut motility as well as gut sensation. As mentioned, if a WMC test shows normal gut motility/normal gut transit, then the doctor can feel much more confident that a sensory aspect and significant gut-brain interaction is contributing to the patient's symptoms. The normal WMC test result more strongly suggests that there is a disorder of gut-brain interaction that has to be focused on and treated.

My colleagues and I looked at 5 different patient cohorts who presented with some form of GI symptoms to try to figure out what percentage of them had a gut transit abnormality. It turns out that among all symptomatic patients, even those who had a previous abnormal gut transit test, generally, an abnormality was found in approximately 30% after objective measurement (eg, of all patients who present with upper GI symptoms, about 30% of them have documentable upper GI delay). What is intriguing is that of the 30% with an abnormality in the upper GI tract, another 30% also had a concomitant lower GI issue. Patients may or may not say they have both upper and lower GI symptoms. This is because the GI tract is one integrated long tube, and disorders of

gut-brain interaction tend to be indolent. It is important that abnormalities can be measured because at least if we identify these abnormalities, whether they are silent or not, they are targets that can potentially be treated. There are medications to treat delayed colonic transit in someone who also has delayed upper GI transit. Studies have shown that when lower GI transit delay is treated, even in patients with no lower GI complaints, their upper GI symptoms improve. This double improvement is possible with appropriate treatment after objective measurement with WMC testing.

Those who benefit are patients with symptoms in whom we can identify an abnormality or multiple abnormalities that can be targeted with treatment in the hope of making them better. Another important group, as I emphasized, consists of those who have symptoms but no abnormality in whom the focus is not on trying to improve GI motility but on helping patients feel better by reducing symptoms with medications that change the nerve ending sensitivity. The consideration of treatment when there is no objective evidence of an abnormality is an extremely important step that is often ignored. Neuropathic pain treatments can be considered.

G&H Are there any contraindications to WMC testing?

BK The capsule must be swallowed and is about 2.8 cm long and 1.17 cm wide, which some patients have difficulty swallowing. In addition, patients who have a history of stroke or a medical disorder that makes it difficult to swallow regular food may be unable to swallow the capsule. Another major contraindication is patients at risk for capsule retention. Unlike how an endoscopist can maneuver the endoscope around an impassable area or remove the endoscope, when the free-floating capsule encounters a stricture or blockage and becomes stuck, it will not come out without an invasive procedure. Although this may seem like a drawback, it serves a twofold purpose: (1) it ensures that the gastroenterologist who orders WMC testing has ruled out any potential blockage as the cause of the patient's symptoms by performing endoscopy and possibly radiology, and (2) a capsule that becomes stuck is an actionable finding. It is unfortunate when a blockage is detected that way, but it provides an opportunity to address the cause of the patient's symptoms. Endoscopy or an operation to remove the capsule and repair the offending area can be performed in the hope that the patient will feel better.

In general, I tend to avoid giving capsules to patients who have had major bowel luminal surgeries, not because I am worried about capsule retention in these patients but because the normal values for WMC testing are based on people who have not had any major bowel luminal surgery. For patients who have had gastric bypass or gastric sleeve surgery, the capsule information for the stomach may be impossible to interpret; however, the clinician can probably interpret the information in the other unoperated areas of the GI tract. Likewise, for the patient who had a partial or total colectomy, the colon results may be uninterpretable, but the upper GI results may be helpful. Bowel surgeries are not necessarily absolute contraindications; however, part of the capsule test results from the affected bowel will not be interpretable because we have no standards for evaluating the bowel after surgery and do not expect to have any for this.

G&H What are the adverse events of WMC testing?

BK Occasionally, patients may not be able to swallow the capsule because of dysphagia or phobias. There have not been any significant documented cases of aspiration. In patients with a severe motility issue, which may be the primary reason for the study, the capsule may remain in the stomach for more than 2 or 3 days or, possibly in the worst-case scenario, at the end of the 5- or 8-day monitoring period. In this case, the capsule, which is radiopaque, can be located with a plain x-ray. If the capsule is in the small intestine, barring any type of obvious blockage preventing the outflow, patients are treated with laxatives similar to a bowel preparation. In the few instances when a capsule had not passed, it was removed from either the stomach or the colon. A capsule retained in the stomach because of poor motility is valuable information. If the stomach capsule does not empty after 10 to 15 days, frankly, the prognosis is poor, as the patient may need nutrition either directly into the small intestine or intravenously.

G&H How has the SmartPill and Atmo Capsule experience informed development of new capsule technology?

BK The SmartPill showed that pH and pressure could give a vast amount of information about transit and contractility and how there can be multiple areas of GI tract involvement. This was attained with one pressure sensor. Questions being considered are whether more sensors on the capsule would provide even more information, whether 2 sensors spread out enough would show a ripple of contractions over the capsule, and whether additional sensors measuring other aspects, besides pH, pressure, and temperature, could not only sense the environment but possibly even sample the environment in different ways. There are a number of ingestible capsules with sampling

technologies in development for other disease processes.

The Atmo Capsule is intriguing because it provides accelerometer information, indicating whether the capsule is wobbling or flipping around, and this movement provides a circuit measure of pressure contractions in the GI tract. It does not measure pressure directly but rather measures the impact of the contractions on the capsule, so the Atmo Capsule has shown that measurements of gut motility in addition to transit can be obtained by different means. Gas-sensing technology could potentially be useful in the evaluation of patients who have different forms of malabsorption or bacterial overgrowth to sense the gas differentials in these populations; however, that remains to be further evaluated.

For what else can be packed into the WMC, there is an amazing universe to consider.

The experience so far highlights that the capsule with its sensors (whether pressure, temperature, pH, gas, or accelerometer) is a conveniently packaged ambulatory device, known to be relatively safe in a wide population of patients. For what else can be packed into the WMC, there is an amazing universe to consider.

G&H Are ingestible capsules that deliver medication within the GI tract the next step?

BK It is a consideration. There is a capsule technology labeled as a medical device that delivers vibrational frequencies to treat constipation that is already FDA approved. This may be the first example of a capsule technology moving from a diagnostic category to a therapeutic one. Many patents have been submitted for capsule technology that delivers a small payload of medication to a specific area. Potentially, if the location could be pinpointed by pH, gas, or possibly even specialized telemetry and echolocators, then the physician might be able to drop a specific amount of therapeutics onto the most diseased area. Use of a capsule as a vehicle for delivering pharmaceutical options in this way could decrease the amount of drugs needed with potential systemic side effects.

G&H What should future research focus on?

BK First, capsule technology can be used to help us understand better the pathophysiology underlying how the GI tract operates in health and in disease. Because it is noninvasive and allows us to study a greater number of patients (both healthy volunteers and patients with all sorts of GI conditions), the capsule has an advantage over radiology-based or catheter-based technologies, which are limited by the amount of radiation and tubes patients are willing to tolerate. The ease of WMC testing will likely lead to more physiologic insights, adding to the knowledge of GI physiology published in studies on the SmartPill WMC. Another area of future research could be on whether the capsule can evaluate pharmaceutical impact, such as treatments for disorders of gut-brain interaction. How does treatment improve the gut physiology or gut transit? Patients may say they feel better or say they do not feel better, but that is not necessarily objective evidence. Capsule technology can provide proof that our efforts are having an impact on patient gut physiology. Lastly, further research on how to take capsule technology beyond the diagnostic to the therapeutic level is an area with immense growth potential.

Disclosures

Dr Kuo is a consultant for Given, Medtronic, and Atmo Biosciences. He is also a principal investigator for the SmartPill and Atmo Capsule clinical trials.

Suggested Reading

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