

Imaging capsule: Does it represent a real progress?

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Identification and confrontation of small bowel (SB) disorders remains a difficult problem in daily clinical practice. The small bowel has been labelled the black box of obscure bleeding because trying to identify the bleeding source can frequently be frustrating. Also, the diagnosis of Crohn's disease, small bowel tumours and polyps and evaluation of patients with small bowel diarrhea is often delayed.

Push enteroscopy remains a useful method for examining the SB. It has the advantage of visualizing subtle mucosa changes, taking biopsies and allowing endotherapy. However, its inability to examine the SB beyond the proximal jejunum and other disadvantages (including the need for sedation, patient intolerance and possible complications) prevent it from being characterized as the "gold standard". The other two available endoscopic methods, which could examine the entire SB, namely sonde and intraoperative enteroscopy, have certain technical limitations. Other diagnostic methods, including angiography, scanning techniques and computed tomography, are helpful in a limited number of clinical settings. Barium studies, i.e. SB follow-through and enteroclysis, are often used for the evaluation of suspected SB diseases in daily clinical practice, with the latter to be considered the radiological study of choice. Although the diagnostic yield of enteroclysis in patients with SB tumours is high, in unexplained GI bleeding it is dismal (up to 20%).

Recently, a new method has been developed, i.e. wireless capsule endoscopy (WCE), enabling non-invasive diagnostic endoscopy of the SB and permitting the direct visualization of the entire small intestinal mucosa during its normal peristalsis. WCE was developed in or-

der to overcome the existing difficulties in the evaluation of patients with suspected SB disorders.

WCE has certain advantages compared to the above mentioned methods of diagnosis of SB diseases; it permits pain-free direct visualisation of the entire length of the SB mucosa, from the duodenum to the ileocecal valve, and the capsule may be given to critically ill patients and patients with severe cardiological problems in whom push enteroscopy would be undesirable.

The wireless capsule endoscope (The Given Diagnostic Imaging System, M2A™ capsule, Given Imaging, Yoqneam, Israel) has a cylindrical shape, with a diameter of 11mm and a length of 26mm. It has two convex domes, one of them being the optical dome and it contains 4 LEDs (light emitting diodes), a lens, a colour camera chip, two batteries, a radio frequency transmitter and an antenna. The capsule obtains two images per second and transmits the data via radio frequency to a recording device worn about a patient's waist. Once the acquisition time is reached, the data from the recording device is downloaded to a computer workstation (2h 30') whose software processes the images for viewing on the computer screen. Averages of 50000 images are obtained during an eight-hour examination.

Review of the images should be performed by individuals who are experienced in viewing and interpreting endoscopic images. The reading time, at least in the beginning, is a time-consuming process, lasting from 90 minutes to 2 hours (or even more). After performing a small number of examinations and proper training, the reading time shortens. In our Department, after accumulating experience of 200 cases, we are now able to read capsule endoscopy images in 40-60 minutes.

Bowel preparation in WCE remains an ongoing problem, often leading to the need to repeat WCE; this eventually increases the total cost of the method. Although PEG solutions improve the quality of acquired images (especially those from the proximal SB), in many cases

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this improvement does not seem to be sufficient for the imaging of the distal SB; therefore further studies seem to be necessary, in order to address this issue.

Indications for WCE continue to be undefined. Capsule endoscopy has rapidly gained acceptance as a diagnostic tool to evaluate obscure gastrointestinal bleeding, and has been shown to have a higher diagnostic yield compared with push enteroscopy, small bowel follow-through and enteroclysis. The diagnostic value seems to be higher in obscure overt bleeders (melena or hematochezia) compared to obscure occult bleeders (heme positive stool test or iron deficiency anemia). Angiodysplasias were found to be the most common cause of obscure GI bleeding. However, to date, it remains unclear whether WCE alters the long-term, clinically relevant outcomes in this patient population; we therefore await studies of this kind with great interest.

In addition to the identification of obscure intestinal bleeding, WCE may prove to be a useful tool in indentifying nonsteroidal anti-inflammatory drug (NSAID)-induced mucosal abnormalities, evaluation of patients with known or suspected Crohn's disease, polyposis syndromes and, less likely, intestinal malabsorptive disorders and chronic abdominal pain. Regarding Crohn's disease, WCE seems to have an important role in its detection and treatment. Studies have shown that WCE was able to expand the extent of the disease in a half of patients with known Crohn's disease; which findings led to clinically beneficial diagnostic changes and improved patient care.

Nevertheless, Crohn's disease it is a compounded diagnosis which relies heavily on clinical presentation, endoscopy, radiology and histology. There is no single hallmark which can offer us the absolute certainty that we are dealing with Crohn's disease. Even histology may not provide a complete proof, although it can obviously be an important part of the puzzle. Thus, quite frequently there is a delay between the onset of symptoms and the diagnosis of the disease in actual clinical practice. Patients with persistent symptoms, such as chronic diarrhea for years and/or iron deficiency anemia despite negative conventional workup, are therefore common in this field. Fireman et al. studied the effectiveness and diagnostic yield of WCE in patients with suspected Crohn's disease of the SB undetected by conventional modalities. Of the 17 study participants, 12 (70.6%) were diagnosed as having Crohn's disease of the SB according to the findings of the M2A Given capsule, giving the promise that it could be an effective modality in this group of patients; these findings have been confirmed by other studies. It

is important to note that these were patients without anemia, no sedimentation rate elevation and the physician would otherwise think that they might have irritable bowel syndrome instead of Crohn's disease. Thus, it will be important to revisit the question of the true incidence and prevalence of Crohn's disease, whether patients with SB lesions actually improve if we treat them or whether these findings are without any clinical significance.

As we begin to identify the role of WCE in celiac disease, we can say that WCE appears to have a high yield in symptomatic patients with celiac disease while on a gluten free diet. The most important finding by WCE in this group of patients was multiple ulcerations, distributed in the jejunum and ileum, occurring mainly in patients with abdominal pain, suggestive of ulcerative jejuno-ileitis.

In patients evaluated by WCE for unexplained abdominal pain, the clinical implication of WCE is still questionable. "Suggestive findings" are common; however, the clinical significance of these findings needs to be better delineated before WCE can be recommended for this indication.

Clinical implication of WCE in a number of disease models (such as eosinophilic gastroenteropathy, immunodeficiency syndromes, graft versus host disease (GVHD), chemoradiated patients, SB transplantation), are still under evaluation, giving the promise that it might be useful in the future.

The experience from WCE in pediatric population is still limited. Young children may hesitate to swallow the capsule; this seems to be one of the limitations of WCE in the pediatric age group. As the gold-standard studies are different in children as compared to adults (push enteroscopy is rarely performed in pediatrics), we await with great interest specially conducted studies, in order to evaluate the safety, tolerance and clinical value of WCE in certain pediatric groups.

Contraindications for WCE are: intestinal obstruction or strictures, swallow disorders, patients with cardiac pacemakers or implanted defibrillators and pregnancy. The worldwide reported percentage of capsule non-passage, requiring surgical intervention, is less than 1%. Strictures secondary to Crohn's disease, NSAID-induced, radiation-induced strictures and post-surgical narrowing, have been identified as the main causes of capsule non-passage. Although a variety of methods for identification of intestinal strictures are used, they all have a very limited accuracy. If however we look at ongoing trials of

WCE in patients with known Crohn's disease (CDAI >200) with an exclusion criteria of intestinal strictures less than 10mm in diameter, as determined by radiological studies, the results show that more than 50% of the patients would have to be excluded.

This experience has created a need for an "M2A™ Patency System" with intended use to detect strictures or obstruction within SB. This capsule is mainly made of a lactose body very similar to conventional capsules for pharmaceutical purposes, mixed with 5% barium, which allows it to be radio-opaque. The capsule has a timer plug at its tip with an exposed window allowing penetration of intestinal fluid through this window. At a preset time of about 100 hours, when sufficient fluid has entered the capsule, it disintegrates. The metallic tag in the center of the capsule, covered by a polyamide coating, is very small, with diameter of 2mm and length of only 10mm. The first human trials using the M2A Patency System, in patients with known SB strictures, were very hopeful.

WCE is also contraindicated for use in patients with a cardiac pacemaker or implanted electro-medical devices. Nevertheless, there are reports in the literature of no observed interference between WCE and bi-polar cardiac pacemakers, and vice-versa. We must point out that we have had the same experience in a patient with a bi-polar cardiac pacemaker who underwent WCE in our hospital, without any consequence.

In conclusion, WCE is an exciting new diagnostic method, which has come to extend the existing meaning

of endoscopy. Accumulated data show that its usefulness is very high for the evaluation of patients with obscure GI bleeding and known or suspected Crohn's disease. WCE complements the traditional work-up in patients with suspected SB diseases, holding the promise that fewer patients with SB disorders will remain undiagnosed.

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