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Editorial

Virtual chromoendoscopy as an adjuvant to capsule endoscopy: a step ahead?

Gastroenterology has always pursued the non-invasive visualization of the digestive tract in its entirety as an addition to the excellent role played by gastroscopy and colonoscopy in upper and lower gut segments. Capsule endoscopy has no doubt represented a radical change in the practice of endoscopy in our time, as it contributes to solve problems in the assessment of the small bowel. Currently established indications for the use of capsule endoscopy to examine the small bowel include obscure gastrointestinal bleeding (OGIB), the study of unexplained iron deficiency anemia in the upper or lower GI tract, Crohn's disease, polyposis syndromes, and improved identification of abnormal images seen in the small intestine with other techniques (1). Indications currently under assessment include the study of celiac disease, melanoma staging, malabsorption syndrome assessment, graft-versus-host disease, and small bowel transplantation (1).

A capsule endoscope moves along the entire gastrointestinal tract while capturing high-quality images that are then wireless transmitted via an antenna array on the patient's abdomen to an external data recorder held in position by a belt. This is an ingestible cylindrical device fitted with a tiny videocamera, light emitting diode (LED), optical system, semiconductor image sensor, and small battery, all this inside an inert, biocompatible plastic capsule. Lighting LEDs (white light) flash several times per second –depending on capsule type– and illuminate the intestinal wall through a clear optical dome. Images obtained are then reviewed by a gastroenterologist following their download onto the workstation. Images were obtained with white light and could not be modified until recently. The PillCam Given® capsule has been mated to Fujinon's FICE® (Fuji Intelligent Chromo Endoscopy) technology in order to better visualize selected mucosal lesions in the small bowel. FICE is a *"virtual chromoendoscopy"* technology that allows better image/lesion contrast enhancement by using various empirical hallmarks to highlight a number of aspects in the endoscopic image's white light, which will theoretically contribute to improve contrast between suspect lesions and the surrounding mucosa (2). Thus far this *virtual chromoendoscopy* FICE technology has only been used for the study of esophageal, gastric, and colonic lesions in association with a gastroscope or colonoscope rather than a capsule endoscope (3,4). FICE, as applied to capsule endoscopy, has currently the limitation that it can only be used for static images, that is, an image can only be software-processed once downloaded and saved onto the workstation but not in vivo during intestinal transit. In the future FICE as applied to capsule endoscopy should be naturally expected to work as it currently does for conventional endoscopy. However, in contrast to conventional chromoendoscopy using stains, FICE represents a convenient, simple, fast tool that allows image acquisition by merely pressing a key at the workstation. It should be underscored that FICE requires no structural changes in a capsule endoscope, which

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facilitates implementation in clinical practice (5). FICE offers three types of pre-adjusted settings (designated 1, 2, and 3) according to the wavelength that is enhanced. The usefulness of these three frequencies during capsule endoscopy is still under assessment.

Evidence contained in the literature on this topic is limited, and the few publications that discuss the combined use of capsule endoscopy and FICE have focused on patients with obscure gastrointestinal bleeding (OGIB), as this is the most common and established indication for this technique (6,7). Capsule endoscopy is usually chosen following upper endoscopy and colonoscopy with terminal ileum intubation. The diagnostic yield of capsule endoscopy in this setting has been estimated to be around 60%, hence a wide margin for improvement exists in this field and some researchers have posited that FICE might well help improve performance. This fact would primarily result from better visualization for two lesion types: a) aphthous lesions, erosions or ulcers; and b) angiodysplasia-like vascular lesions. When using FICE on aphthous lesions images gain improved definition, lesion edges are sharpened, and peripheral inflammation halo visualization is enhanced. Vascular lesions are also highlighted by FICE, which adds contrast and provides reddish areas with increased depth and better delimited borders. All in all, FICE might seemingly become a new valuable tool for gastroenterologists, allowing a better, more extensive visualization of the aforementioned lesions. Currently, studies show that capsule endoscopy is superior to double-balloon enteroscopy for diagnostic purposes and should be performed first, followed by double-balloon enteroscopy with a therapeutic aim only when warranted by capsule endoscopy findings (8-10).

Gupta et al. retrospectively examined a cohort of 60 patients with OGIB who had a capsule endoscopy procedure (aided by FICE technology). The authors concluded that FICE allowed no enhancements for results obtained with white light for the diagnosis and characterization of lesions in this type of patients. FICE could not increase the diagnostic yield –while able to detect more intestinal lesions, the latter had no clinical relevance. However, it did allow a better characterization of selected vascular lesions by color intensification and better edge definition (11).

Imagawa et al. retrospectively assessed 145 static images of small bowel mucosal lesions from 122 patients that were enhanced with FICE, and concluded that this technology allowed a better visualization of angiodysplasias, erosions/ulcers and tumors (12). However, these same authors, in a prospective trial including 50 patients, drew different conclusions as they found no significant differences between white light and FICE regarding erosion, ulcer and tumor visualization (13). On the other hand, FICE was particularly useful for angiodysplasia detection (13).

The study reported by Duque et al. (14), in the present issue of *The Espanish Journal of Gastroenterology*, is particularly interesting as it provides further scientific evidence on this topic, which will help in drawing clearer, more deeply rooted conclusions. Nevertheless, while this is a prospective, controlled study, its limited size precludes definitive conclusions. As the authors report, experience with capsule endoscopy and FICE is limited even for specialist teams in the study of the small bowel, and so a greater number of examinations is needed to gain deeper insight into this technique. On the other hand, importantly, the fact that not all findings visualized during endoscopy will necessarily have clinical relevance should be borne in mind. Duque et al. (14) describe all their findings but we do not know the number of patients in whom such findings significantly modified their therapeutic attitude. This is a crucial aspect since clinical validity and the future of chromoendoscopy techniques rely in their significant contributions to improved medical management, especially in complex patients such as those with OGIB. That is, of a chromoendoscopy technique we should

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not only ask for high-quality images but also key data allowing to significantly modify clinical management for patients.

Other aspects to be elucidated in the next few years regarding capsule endoscopy in association with FICE include: cost-effectiveness assessment, a comparison of time devoted to conventional capsule endoscopy *versus* FICE-enhanced capsule endoscopy, establishing the most appropriate bowel preparation for this type of exam and which predetermined FICE settings would allow the best image quality (15).

In summary, the data published by Duque et al. (14) are highly relevant from a clinical standpoint, but we consider prudence is due in their assessment because of the above-mentioned reasons. We deem it appropriate to continue research in this area given its huge potential and promising results, and consider the performance of multicenter studies desirable to definitely and conclusively evaluate the role of this modern technology, from which our patients will benefit no doubt in the near future.

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