Techniques in Gastrointestinal Endoscopy (2011) 13, 2-7

Techniques in
GASTROINTESTINAL
ENDOSCOPY
www.techgiendoscopy.com

Image-enhanced endoscopy

Tohru Sato, MD

Gastrointestinal Endoscopy Unit, Veterans Affairs Palo Alto Health Care System, Palo Alto, California.

KEYWORDS:
Narrow band imaging;
Lugol's solution;
Indigo carmine;
Chromoendoscopy;
Chromoscopy

White light endoscopy is a basic tool available to gastroenterologists since the early 1960s, when flexible endoscopy was first introduced. Since then, gastroenterologists have been able to diagnose and treat gastrointestinal diseases at earlier stages. However, recent studies have also highlighted the limitations and imperfect nature of white light endoscopy. Image-enhanced endoscopy (IEE) has been available for the past 10 years and has been validated by research and clinical trials. A specific combination of dye-based (Lugol's solution, indigo carmine) and equipment-based IEE (narrow band imaging, Fujinon Intelligence Color Enhancement, Pentax i-Scan) is indicated for use in the oropharynx, hypopharynx, esophagus, stomach, and colon. The main use is for detecting, diagnosing, and treating early dysplastic lesions found during screening or surveillance of high-risk patients (eg, Barrett's esophagus, inflammatory bowel disease, hereditary nonpolyposis colorectal cancer syndrome). Effective use of IEE can improve patient prognosis. In this review, we aim to give a concise review of the indications, supportive evidence, and practical guidelines for the use of IEE to improve current diagnostic and therapeutic capabilities. Published by Elsevier Inc.

Gastrointestinal cancers are the second leading cause of cancer-related deaths in the United States,[1] and early detection is critical for better clinical outcomes. Endoscopy is the most sensitive technique for detecting early lesions; however, studies indicate that missed lesions are an important complication.[2] Furthermore, early lesions are subtle and difficult to detect. Fortunately, the technology is improving and research is enhancing white light endoscopy, allowing gastroenterologists to better differentiate normal from dysplastic lesions. Two methods are available for enhancing the contrast between normal and abnormal: dye-based and equipment-based image enhancement. Image-enhanced endoscopy (IEE) is the clinical application of these 2 methods. This paper aims to give a concise summary of the current indications, supporting evidence, and practical steps for implementing IEE (for a more comprehensive review see Ref. 3).

Techniques of IEE

Dye-based IEE techniques

The 2 most commonly used dyes (Lugol's solution and indigo carmine) have different mechanisms for enhancing contrast between normal and abnormal tissue. Lugol's solution is a vital dye that is taken up by normal but not neoplastic or inflamed tissue. The dye is composed of iodine and potassium iodide and prepared as a 2% solution by mixing 8 mL of 5% Lugol's solution (Humcon Co., Texarkana, TX) with 12 mL of sterile water immediately before use. It is most effectively used in the esophagus and anal canal to detect early squamous dysplasia. Normal glycogen granules take up the stain, making normal tissue stain brown in contrast to the pale neoplastic tissue. Using a specialized catheter sprayer (Olympus Corp, Allentown, PA or Cook Medical Inc, Bloomington, IN), 10-20 mL is sprayed evenly over the area of concern detected under white light. After excess stain is suctioned, the marked area is biopsied immediately because staining is transient. Because Lugol's stain may induce some submucosal fibrosis, if endoscopic resection is planned we generally delay the application of the Lugol's until the time of the resection procedure. Lugol's stain provides a clear delineation of the dysplasia from normal squamous epithelium and allows precise peripheral

The authors report no direct financial interests that might pose a conflict of interest in connection with the submitted manuscript.

Address reprint requests to Tohru Sato, MD, 3801 Miranda Ave, GI-111, Palo Alto, CA 94304. E-mail: tohru.sato@va.gov

1096-2883/11/$-see front matter Published by Elsevier Inc.
doi:10.1016/j.tgie.2011.01.010

Table 1 Tools for image enhanced endoscopy

1. High-resolution or high-definition endoscope
2. Distal translucent cap (Olympus, Tokyo, Japan)
3. Diluted simethicone
4. Lugol's solution: 2% solution is made by mixing 8 mL of a 5% solution (Humcon Co) with 12 mL of sterile water
5. Indigo carmine: 0.2% dilution is made by mixing 5 mL of an 0.8% solution (American Reagent Laboratories) with 15 mL of water
6. 60-mL syringe
7. Spray catheter

marking of the lesion. Side effects are rare but documented to include retrosternal pain, nausea, chemical esophagitis, and chemical pneumonitis. The equipment needed is listed in Table 1.

Indigo carmine is a contrast dye that is not taken up by tissue but fills the pits, grooves, and depressions of columnar mucosa to aid in delineating the borders and surface topography of a lesion. The dye is a blue, plant-based dye and is used as a 0.2% solution made by mixing 5 mL (1 ampule) of a 0.8% solution of indigo carmine (American Reagent Laboratories, Inc, Shirley, NY) in 15 mL of sterile water. The dye is most effective in detecting dysplastic tissue in Barrett's esophagus[4] and nonpolypoid colorectal neoplasms in the colon.[5] The solution is applied by 60-mL syringe directly injected into the accessory channel of the endoscope and onto the potential lesion. In cases of surveillance colonoscopy for inflammatory bowel disease, the dye is used as a more dilute solution by mixing 10 mL (2 ampules) of a 0.8% solution in 250 mL of sterile water. This solution is sprayed onto the colonic mucosa using a water jet to cover a large area and facilitate the detection of dysplastic tissue. Side effects have not been reported except for transient green-hued urine if large amounts are sprayed or injected.

Equipment-based IEE techniques

Three main devices use equipment-based IEE: Fujinon Intelligence Color Enhancement, narrow band imaging (NBI) by Olympus, and Pentax i-Scan. All 3 enhance the image from the endoscope by increasing the contrast between hemoglobin (ie, highlighting the vasculature) and normal tissue because early lesions and dysplastic tissue have increased vascularity and alterations in the morphology of their microvasculature.[6] The images are altered either precapture (altering the light source) or postcapture (altering the captured image). Fujinon Intelligence Color Enhancement uses postcapture technology and enhances the endoscopist's view by creating a series of "spectral images," which are images created by selectively processing specific wavelengths of light. NBI uses precapture technology and creates an enhanced image by emitting only blue (415 nm) and green light (540 nm). The blue light is most efficiently absorbed by hemoglobin, making vascular structures dark and thus easily detected and characterized in terms of their size, density, and configuration. Pentax i-Scan uses postcapture technology and separates the captured image into its red, green, and blue components and reconstitutes an image, maximizing surface enhancement, contrast enhancement, or tone enhancement. There is also an added feature that allows unenhanced and enhanced images to be viewed side by side to more easily identify the area of interest. Each of these systems is currently available and able to be engaged and disengaged by the touch of a button.

Clinical application

Equipment-based and dye-based IEE methods are both indicated in clinical use in the hypopharynx, esophagus, stomach, and colon. For each tissue, a specific combination of modalities, although not all, is useful for enhancing diagnosis and management.

Hypopharynx (NBI)

IEE is indicated for the inspection of the oropharynx and hypopharynx in patients at increased risk for squamous cell cancer of head and neck (ie, patients with a history of tobacco use, heavy alcohol use, history of head and neck cancer, or squamous cell cancer of the esophagus). NBI can highlight precancerous and early cancers of the head and neck—early lesions are well-demarcated brown areas with tiny dots, indicative of dysplastic squamous epithelium with irregular foci of microvascular proliferation.[7,8] NBI is more sensitive and accurate than white light imaging in detecting superficial cancers in the head and neck and esophagus in a multicenter, prospective, randomized controlled trial of 320 patients with a history of esophageal squamous cell carcinoma.[9] At our hospital, we inspect the hypopharynx under white light and scrutinize areas that are slightly redder under NBI with magnification. If the area has the typical findings described above, we biopsy or remove by endoscopic mucosal resection the area of concern, depending on the expertise of the endoscopist (Figure 1).

Esophagus

Squamous Cell Carcinoma (Lugol's/NBI)

In the esophagus, Lugol's solution and NBI are indicated in individuals at high risk for squamous cell cancer (ie, history of alcohol abuse, heavy tobacco use, lye ingestion, or head and neck cancer).[10,11] Lugol's solution increased the diagnostic yield for high-grade dysplasia and cancer by 20% in a study of 1095 high-risk patients.[12] The test is sensitive, with up to 26% of a cohort of 629 patients having unstained lesions, but limited by its low specificity—only 3% of the patients were diagnosed with cancer.[13] Equipment-based IEE in tandem is a potential way to increase specificity. NBI can reveal the unique surface features of early cancers. These lesions have distorted intrapapillary capillary loops, vessels that are associated with high-grade dysplasia and can predict the depth of invasion of superficial lesions.[14]