Chromoendoscopy

Raquel E. Davila, MD

KEYWORDS

• Chromoendoscopy • Dye spraying • Staining
• Barrett's esophagus • Dysplasia • Esophageal cancer
• Gastric cancer • Colorectal polyps

Chromoendoscopy involves the topical application of stains or dyes to the gastrointestinal mucosa during endoscopy to improve tissue visualization, characterization, and diagnosis.[1] Stain or dye solutions are categorized as absorptive (vital), contrast, or reactive. Absorptive stains are taken up by specific epithelial cells of the gastrointestinal tract. Contrast stains are not absorbed, but rather pool in the crevices of the mucosa and accentuate the topography and mucosal irregularities of tissues. Reactive stains respond to the chemical milieu within tissues and undergo a color change based on the presence of an acidic or alkaline pH.

TECHNIQUE AND SPECIFIC STAINS

Stain solutions are generally widely available. Dilution of the staining agents may be necessary, as they are often commercially available in concentrated form. A dedicated spray catheter is usually used through the working channel of the endoscope to deliver a fine mist of the staining solution to the mucosa. Intravenous glucagon or atropine may be used before stain delivery to decrease motility and optimize visualization.

Lugol's Solution

Lugol's solution is an absorptive stain containing iodine, potassium iodide, and distilled water. The solution has an affinity to glycogen in nonkeratinized squamous epithelium, and, therefore, is usually used in the esophagus to detect squamous dysplasia and squamous cell carcinoma.[2,3] Application of a 0.5% to 3% solution to the esophagus results in a green-brown, dark-brown, or black discoloration of the mucosa lasting up to 5 to 8 minutes. Absence of staining results from conditions in which there is depletion of glycogen in squamous cells, such as dysplasia, squamous cell carcinoma, Barrett's epithelium, and inflammation. Intense uptake of the stain can be seen in areas of glycogenic acanthosis.[4]

The free iodine component of the Lugol's solution can cause mucosal irritation, leading to oropharyngeal burning, retrosternal pain, erosive or ulcerative esophagitis, and, rarely, erosive gastritis.[5,6] The topical application of a sodium thiosulfate solution at the end of the endoscopic procedure has been reported to significantly reduce

VA North Texas Health Care System, University of Texas Southwestern Medical Center, 4500 S. Lancaster Road, MC 111B1, Dallas, TX 75216, USA
E-mail address: raquel.davila@utsouthwestern.edu

Gastrointest Endoscopy Clin N Am 19 (2009) 193–208
doi:10.1016/j.giec.2009.02.005 giendo.theclinics.com
1052-5157/09/$ – see front matter. Published by Elsevier Inc.

symptoms after Lugol's staining.[7] Use of the stain should be avoided in patients with iodine sensitivity. Severe allergic reactions have been reported, including bronchospasm in a patient with asthma.[8]

Methylene Blue

Methylene blue is an absorptive stain that is actively taken up by normal, absorbing intestinal epithelial cells of the small intestine and colon. The stain is not taken up by nonabsorptive cells, such as normal gastric or squamous epithelium, but is absorbed by intestinal metaplasia of the esophagus[9] and stomach.[10] Weak or absent staining in the small intestine, colon, or in areas of intestinal metaplasia is indicative of dysplasia, neoplasia, or inflammation. Methylene blue staining has been primarily used in the detection of specialized intestinal metaplasia, dysplasia, and early cancer in Barrett's esophagus. It has also been used in the detection of intestinal metaplasia, dysplasia, and early cancer of the stomach.[10–13]

Chromoendoscopy with methylene blue in the esophagus involves several steps.[14] First, the surface mucus is removed using a mucolytic agent, such as a 10% solution of N-acetylcystein. After approximately 2 minutes, a 0.5% to 1% solution of methylene blue is applied. Staining occurs within 2 to 3 minutes, and excess dye is then vigorously removed with water irrigation. Epithelial uptake of the stain results in a blue discoloration, which is resistant to washing and can persist for up to 24 hours. Excretion of the stain can occur through the urinary tract or by cellular sloughing into the gastrointestinal tract, which can result in greenish or bluish discoloration of the urine and stool.[1,15]

In general, methylene blue is well tolerated, with no significant side effects reported. There have been reports of oxidative DNA damage induced by the combination of methylene blue and white light exposure during chromoendoscopy of Barrett's epithelium and colonic mucosa.[16,17] It has been speculated that this DNA damage can accelerate carcinogenesis in Barrett's epithelium. However, there is no current evidence of increased cancers in patients who have undergone chromoendoscopy with methylene blue in clinical studies.[18]

Toluidine Blue

Toluidine blue or tolonium chloride is a basic dye that stains cell nuclei.[1] It is mostly used in the detection of malignant cells due to their increased mitotic activity and high nuclear to cytoplasmic ratio, which lead to avid stain absorption.[19] Staining of abnormal tissues results in blue discoloration. Toluidine blue chromoendoscopy has been mainly used in the evaluation of squamous dysplasia and squamous cell carcinoma of the oral cavity and esophagus.[20–23] Benign conditions, such as inflammation, erosions, ulcers, and fibrosis, can falsely stain positive.[1,4]

The staining technique involves use of a mucolytic, such as 1% acetic acid, to get rid of surface mucus. Subsequently, a 1% aqueous toluidine blue solution is sprayed topically. After 1 to 2 minutes, a second washing with 1% acetic acid is performed to remove any excess dye.[21] There are no reports of side effects or toxicity associated with toluidine blue use.

Crystal Violet

Crystal violet is a topical antimicrobial agent that irreversibly binds microbial DNA and directly inhibits cell replication.[24] It stains the nuclei of normal and cancerous cells, resulting in a purple discoloration, and is useful for highlighting the surface morphology of cells. Crystal violet staining has been reported to be useful in delineating the pit