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MINI REVIEW

The role of acetic acid in the management of Barrett's oesophagus

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Summary Barrett's oesophagus is of significant importance due to its premalignant potential. Acetic acid chromoendoscopy is a simple technique that can be used with any endoscope system. It has been utilised for the identification of Barrett's intestinal metaplasia; and more importantly, for the localisation of early neoplasia within Barrett's, which is often focal, subtle and very easy to miss by random quadrantic biopsies alone. Acetic acid is routinely utilised in specialised centres and its use is expanding. This article examines the evidence base behind acetic acid chromoendoscopy and looks at where further research needs to be directed.

Introduction

Barrett's oesophagus is a very common finding during upper GI endoscopy, being found in approximately 6—12% of patients undergoing endoscopy for symptomatic gastro-esophageal reflux disease [1]. It is currently defined by most endoscopy societies as the presence of metaplastic columnar epithelium of any length in the distal oesophagus. American guidelines require the presence of IM in columnar lined oesophagus (CLO) before a diagnosis of Barrett's oesophagus can be made, whilst in British guidelines, columnar lined oesophagus (CLO) is considered to be adequate for the diagnosis. It is however universally recognised that the presence of intestinal metaplasia (IM) confers increased cancer risk and that IM is present in the vast majority of long segment Barrett's.

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The importance of Barrett's oesophagus lies in the fact that it has been established as a high-risk condition for the development of oesophageal adenocarcinoma. The incidence of oesophageal adenocarcinoma is rising in the western world [2,3]. It is responsible for 14,500 deaths per year in the United States [4] and 7000 per year in the United Kingdom [5]. Barrett's oesophagus is easily accessible through the endoscope and early cancerous changes can be diagnosed by endoscopy and histology. The presence of intestinal metaplasia within columnar lined oesophagus also increases the risk of neoplastic transformation. The best way of reducing mortality related to adenocarcinoma is to diagnose Barrett's neoplasia at an early stage. For this reason, most gastroenterology societies in the west recommend regular surveillance for Barrett's oesophagus, with a view to early cancer and dysplasia detection and therefore improved survival.

Conventional surveillance protocols involve taking multiple random quadrantic biopsies at 1 cm (Seattle protocol) or 2 cm (Cleveland protocol) intervals. This has remained standard practice as most dysplastic areas are difficult to visualise with standard resolution white light endoscopes and only 13% of early neoplastic lesions appear as macroscopically visible nodules [6]. However, the poor neoplasia picks up rate during routine surveillance with white light endoscopy and quadrantic biopsies questions the cost-effectiveness of this technique [7]. Intestinal metaplasia, intraepithelial neoplasia and early carcinoma are often distributed focally in small areas of less than 0.5 cm^2 in the distal oesophagus. For this reason, conventional quadrantic biopsy protocols have a basic limitation which cannot be overcome through non-targeted biopsies alone.

Recent developments have seen an improvement in the optical resolution of endoscopes, and new techniques have been developed which improve mucosal visualisation in Barrett's. Chromoendoscopy is a helpful adjunct to endoscopic diagnosis in Barrett's and has been available for many years. Digital or electronic chromoendoscopy techniques include narrow band imaging (NBI) [8] and Fujinon intelligent colour enhancement (FICE) [9]. Dye based chromoendoscopy techniques have employed methylene blue [10], indigo carmine [11] and acetic acid. These techniques enable previously invisible areas of neoplasia to be visualised in greater detail than previously possible.

The aim of this paper is to review the current available literature for the use of acetic acid in Barrett's oesophagus.

Acetic acid

Acetic acid (AA) or ethanoic acid is a weak fatty acid with a pKa of 4.8. A solution freshly prepared from glacial acetic acid, with a pH of 2.5—3.0 is used for in-vivo application. For many years, acetic acid instillation has been used during colposcopy to detect small lesions in the mucosa of the cervix where there is a squamocolumnar junction. This highlights dysplastic areas and enhances the ability to obtain targeted biopsy specimens and detect cervical intraepithelial neoplasia. This technique has been borrowed by digestive endoscopy, where 1%—3% acetic acid was originally used in the oesophagus as a mucolytic agent before staining with toluidine blue, and as an agent for chromoendoscopy and magnification in Barrett's oesophagus and at the gastric cardia.

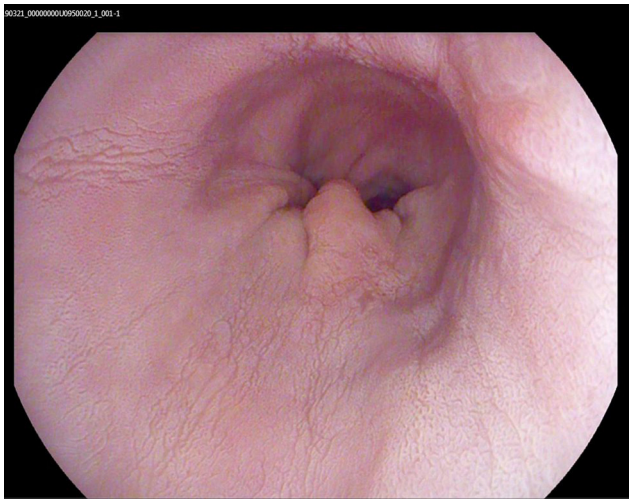

Figure 1 Normal Barrett's acetowhitening.

Mechanism of action

When acetic acid is sprayed onto squamous epithelium, there is an acetowhitening reaction, resulting from increased opacity of the mucosal surface and masking of the submucosal capillaries [12]. Neutralisation of AA as it progresses through multi-layered squamous epithelium protects the subepithelial stroma and vasculature. However, when sprayed on Barrett's epithelium, AA first results in the elimination of the superficial mucus layer by breakage of the disulphide bonds of glycoproteins. The unbuffered acid on the mucosal cell surface then causes a reversible acetylation of cellular proteins and a change in the spatial properties of nuclear and cytoplasmic protiens [12]. This initially produces an acetowhitening reaction (Fig. 1), thus accentuating the surface pit pattern and facilitating detailed examination of the Barrett's epithelium. The transient disruption of the single layered columnar mucosal barrier occurs in a few minutes, leading to mucosal reddening and swelling when the AA reaches the capillaries in the stroma [1,12] (loss of acetowhitening). Dysplastic areas tend to lose acetowhitening faster than non dysplastic areas and this helps to highlight these areas and target them for biopsies or therapy (Figs. 2—6). The process of spraying AA can be repeated if required, without any permanent damage to the oesophageal mucosa.

Acetic acid for visualisation of Barrett's intestinal metaplasia

Acetic acid was first used in Barrett's in 1998, when Guelrud et al. reported the use of AA in visualising remnant islands of Barrett's after endoscopic therapy in 21 consecutive patients (Table 1). In 11 patients (52%), AA demonstrated small remnant islands of columnar epithelium not seen before AA instillation [13].