The oesophageal mucosa in reflux disease - endoscopic appearance and tissue structure

Anders Edebo, Department of Gastrosurgical Research, Institute of Clinical Sciences, The Sahlgrenska Academy at Göteborg University, Göteborg, Sweden

ABSTRACT

Gastro-oesophageal reflux disease (GORD) is very common in especially the western world. The cardinal symptoms are heartburn or regurgitations and are caused by the reflux of noxious compounds from the stomach/duodenum to the oesophagus. The first-choice diagnostic method is endoscopy with the observation of erosions or ulcerations (erosive reflux disease; ERD). However, in approximately 50% no erosions are seen on endoscopy despite typical symptoms. These patients are referred to as non-erosive reflux disease (NERD) patients. In the other end of the reflux disease spectrum are the patients developing complications like strictures or metaplastic transformation, *i.e.* Barrett's oesophagus. The latter is a known precursor to adenocarcinoma of the oesophagus. During the last three decades there is an increasing incidence of adenocarcinoma of the oesophagus but underlying causes are unknown. Risk assessment as well as surveillance regimes are still based on histopathology but there is an urgent need for bio-markers to improve individual predictions. The renin-angiotensin system (RAS) is well known for its importance in fluid homeostasis. During recent years this regulatory system has also been shown to be an important mediator of inflammation and carcinogenesis. Epidemiological studies have also indicated a lowered incidence of adenocarcinoma in patients on anti-hypertensive treatment with angiotensin converting enzyme (ACE) inhibitors.

First, the thesis project addressed the possibility of using the latest advances in endoscopical imaging technology to enhance the diagnostic capability of gastric acid-dependent NERD. A NERD-patient group and healthy subjects were examined by high-resolution magnification endoscopy and seven criteria with potentially diagnostic value were proposed. These criteria were further evaluated by a panel of expert endoscopists. Three of the criteria (triangular indentations, apical mucosal breaks and pinpoint blood vessels) were found to be significantly associated to acidic reflux. However the interobserver agreement between expert endoscopists were found to be poor and therefore they cannot be recommended in everyday clinical practice.

Secondly, the thesis elucidates the geographical distribution of known histo-pathological signs of reflux-induced injury in order to evaluate if there were any location in the aboral oesophagus that were more prone to be injured by the refluxate. The results indicate that there is a *locus majori* in the dorsal aspect of the aboral part of the oesophagus that coincides with endoscopically visible erosions and also with the preferred site of superficial oesophageal adenocarcinomas.

A third objective of this thesis was to investigate the distribution of the RAS in the oesophageal mucosa. The RAS system was explored in healthy subjects and patients with erosive reflux disease as well as Barrett's oesophagus and found to be upregulated in association to both inflammation and increasing grade of dysplasia. Especially ACE was found to be associated to neoplasia and may be considered for future research as a bio-marker-candidate.

Key words: oesophagus, reflux, angiotensin, epithelium, endoscopy

ISBN 978-91-628-7358-5 Göteborg 2007

The oesophageal mucosa in reflux disease - endoscopic appearance and tissue structure

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademin vid Göteborgs Universitet kommer att offentligen försvaras i stora aulan, Sahlgrenska Universitetssjukhuset, Göteborg, Fredagen den 7 december kl. 9.00

av

Anders Edebo

Legitimerad läkare

Fakultetsopponent:
Professor Jean-Paul Galmiche
Institut des Maladies de l'Appareil Digestif,
CHU Hôtel-Dieu, Nantes, France

Avhandlingen baseras på följande arbeten:

I. Edebo A, Tam W, Bruno M, van Berkel A-M, Jönsson C, Schoeman M, Tytgat G, Dent J, Lundell L. Magnification endoscopy for diagnosis of non-erosive reflux disease. A proposal of diagnostic criteria and critical analysis of observer variability.
Endoscopy 2007; 39:1-7

II. Edebo A, Vieth M, Tam W, Bruno M, van Berkel A-M, Stolte M, Schoeman M, Tytgat G, Dent J, Lundell L. Circumferential and axial distribution of esophageal mucosal damage in reflux disease.
Diseases of the Esophagus 2007;20:232–238

III. Edebo A, Casselbrant A, Helander H, Vieth M, Fändriks L.
Esophageal mucosal expression of the renin-angiotensin-system (RAS) in reflux disease.
In manuscript.