DIAGNOSTIC VALUE OF RED PHENOL CHROMOENDOSCOPY IN DETECTION OF GASTRIC H.PYLORI

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BO	**Barrit's eosophagus**
CAGA	**Cytotoxin associated gene A**
CAGPAI	**CAG pathogenicity island**
DUPA	**Duodenal ulcer promoting gene**
EGFR	**Epidermal growth factors**
ELISA	**Enzyme linked immune sorbent assay**
FAT	**Fecal antigen test**
FLAA	**Fllagellis A**
GERD	**Gastroeosophageal reflux disease**
HCPA	**Helicobacter cystein rich protein**
IDA	**Iron deficiency anemia**
ITP	**Idiopathic thrombocytopenic purpura**
LPS	**Lipoplysacharid**
MALT	**Mucosal associated lymphoid tissue**
NPV	**Negative predictive value**
OIP	**Outer inflammatory protein**
OMP	**Outer membrane protein**
PCR	**Polymerase chain reaction**
PPI	**Proton pump inhibitor**

LIST OF ABBREVIATIONS *(CON)*

PPV	**Positive predictive value**
PUD	**Peptic ulcer disease**
RUT	**Rapid urease test**
SABA	**Siliac acid binding protein A**
TK	**Tyrosin kinase**
TNF	**Tumor necrosis factor**
UBT	**Uurea breath test**
VACA	**Vacuolating cytotoxin A**
WGO	**World Gastroentrlogy Organization**

Introduction

Helicobacter pylori is a Gram-negative, microaerophilic bacterium found in the stomach. It was identified in 1982 by Barry Marshall and Robin Warren**(Blaser,et al 2006).**

H. pylori's a helix shape (from which the generic name is derived) is thought to have evolved to penetrate the mucoid lining of the stomach **(Yamaoka&Yoshio 2008) (Brown ,et al 2000).**

More than 50% of the world's population harbor H. pylori in their upper gastrointestinal tract. Infection is more prevalent in developing countries, and incidence is decreasing in western countries **(Yamaoka &Yoshio, 2008).**

Individuals infected with H. pylori have a 10 to 20% life time risk of developing peptic ulcers and a 1 to 2% risk of acquiring stomach cancer***(Marshall &Warren, 1984).***Inflammation of the pyloric antrum is more likely to lead to duodenal ulcers, while inflammation of the corpus (body of the stomach) is more likely to lead to gastric ulcers and gastric carcinoma***(Suerbaum & Michetti, 2002).**

For H. pylori diagnosis, One can test noninvasively for H. pylori infection with a blood antibody test, stool antigen test,

or with the carbon urea breath test (in which the patient drinks 14C- or 13C-labelled urea, which the bacterium metabolizes, producing labeled carbon dioxide that can be detected in the breath)***(Stenströmet al., 2008)***.

However, the most reliable method for detecting H. pylori infection is biopsy during endoscopy with a rapid urease test, histological examination, and microbial culture. None of the test methods are completely safe. Blood antibody tests, for example had sensitivity ranging from 76% to 84%. Some drugs can affect H.pylori urease activity and give false negative results with the urea-based tests. Even biopsy result yield is dependent on the location of the biopsy taking ***(Logan &Walker, 2001).***

Chromoendoscopy provides both a better characterization of mucosal lesions in the gut and an increased diagnostic yield in endoscopic procedures ***(Brown and Baraza , 2010).*** This was originally achieved by applying dyes directly on the mucosa via a spray catheter or through the working channel ***(Hurlstone et al., 2002).***

The use of phenol red for the diagnosis of H.pylori infection was initially described in 1991.

A promising clinical utility of phenol red is for the endoscopic detection of H. pylori infection in the stomach, at least as a complementary technique to the ones that already exist. The bacterial urease produces hydrolysis of urea to ammonia and carbon dioxide which would cause the increase in the pH and the red staining of the infected zones.phenol red turns from yellow to red in a basic pH in the infected zones.Because of its reactive and non-absorptive characteristic,it is rapidly eliminated from the organism through the digestive system, without a report of toxicity***(Hernández-Garcés et al.,2010).***

Aim of the work:

The aim of this study is the diagnostic value in use of phenol red chromoendoscopy in detection gastric H.pylori in comparison to histopathology which is the current standard diagnostic method.

Chapter 1: helicobacter pylori

Helicobacter pylori previously named ***Campylobacter pyloridis***, is a Gram-negative, microaerophilic bacterium found in the stomach. It was identified in 1982 by Barry Marshall and Robin Warren, who found that it was present in patients with chronic gastritis and gastric ulcers, conditions that were not previously believed to have a microbial cause .**(Marshall & Warren 1984).**

H. pylori has a critical role in the development of chronic gastritis and peptic ulcer disease and has been linked to the pathogenesis of gastric lymphoma and gastric adenocarcinoma ***(Ford et al 2004).***

Microbiology:

The genus *Helicobacter* belongs to the subdivision of the Proteobacteria, order Campylobacterales, family Helicobacteraceae, genus Helicobacter, species H.Pylori. To date, the genus *Helicobacter* consists of over 20 recognized species, with many species awaiting formal recognition **(Fox 2002).**

H. pylori is a helix-shaped (classified as a curved rod, not spirochaete), Gram-negative bacterium, about 3 micrometres long with a diameter of about 0.5 micrometres. It is microaerophilic; that is, it requires oxygen. It contains a hydrogenase which can be used to obtain energy by oxidizing molecular hydrogen (H_2) produced by intestinal bacteria **(Olson,et al2002)**. It produces oxidase, catalase and urease. It is capable of forming biofilms and can convert from spiral to a possibly viable but nonculturable coccoid form **(Stark et al 1999).**

Helicobacter species can be subdivided into two major lineages, the gastric *Helicobacter* species and the enterohepatic (nongastric) *Helicobacter* species. Both groups demonstrate a high level of organ specificity, such that gastric helicobacters in general are unable to colonize the intestine or liver, and vice versa. All known gastric *Helicobacter* species are urease positive and highly motile through flagella**.(Yoshiyama, & Nakazawa. 2000).**

Urease is thought to allow short-term survival in the highly acidic gastric lumen, whereas motility is thought to allow rapid movement toward the more neutral pH of the gastric mucosa;

this may explain why both factors are prerequisites for colonization of the gastric mucosa **(Schreiber et al. 2005**).

Upon entry, gastric *Helicobacter* species display urea- and bicarbonate-mediated chemotactic motility toward the mucus layer(**Yoshiyama&T.Nakazawa.2000).**The spiral morphology and flagellar motility then assist in penetration into the viscous mucus layer, where the more pH-neutral conditions allow growth of the gastric *Helicobacter* species **(Schreiber et al. 2004).**

H. pylori possess five major outer membrane protein (OMP) families. The largest family includes known and putative adhesins. The other four families include porins, iron transporters, flagellum-associated proteins and proteins of unknown function. Like other typical Gram-negative bacteria, the outer membrane of *H. pylori* consists of phospholipids and lipopolysaccharide (LPS). **(Kusters , et al 2006).**

The outer membrane also contains cholesterol glucosides, which are found in few other bacteria. *H. pylori* has four to six lophotrichous flagella. All gastric and enterohepatic *Helicobacter* species are highly motile due to flagella. The

characteristic sheathed flagellar filaments of *Helicobacter* are composed of two copolymerized flagellins, FlaA and FlaB **(Rust et al 2008).**

Genome and Virulence factor.

Study of the *H. pylori* genome is centered on attempts to understand pathogenesis, the ability of this organism to cause disease. Two of sequenced strains have an approximately 40 kb-long Cag pathogenicity island (a common gene sequence believed responsible for pathogenesis) that contains over 40 genes **(Baldwin et al 2007).** This pathogenicity island is usually absent from *H. pylori* strains isolated from humans who are carriers of *H. pylori*, but remain asymptomatic**.** The *cagA* gene codes for one of the major *H. pylori* virulence proteins. Bacterial strains that have the *cagA* gene are associated with an ability to cause ulcers **(Broutet et al 2001)** **.**

About 50-70% of *H. pylori* strains in Western countries carry the *cag* pathogenicity island (*cag* PAI) **.**Western patients infected with strains carrying the *cag* PAI have a stronger inflammatory response in the stomach and are at a greater risk