

CLO Antibody Assay - Can It be an Alternate to Endoscopy and Biopsy?

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Itrat Mehdi, Huma Qureshi, Waqaruddin Ahmed, Ghazala Mohyuddin, Syed Ejaz Alam (Pakistan Medical Research Council, Research Centre, Jinnah Postgraduate Medical Centre, Karachi.)

Introduction

Helicobacter pylori a gram negative micro-aerophilic spiral gastric bacterium, was first isolated and cultured in 1982¹. Its role is now well established in the pathogenesis of gastritis, gastric ulcer, duodenal ulcer, non-ulcer dyspepsia (NUD), gastric carcinoma and lymphoproliferative disorders of stomach^{2,9}.

A variety of invasive and non-invasive diagnostic tests are currently available for the identification and confirmation of *H. pylori*^{2,3,10,11}. They all are invaluable in a given setting or pre-condition⁷.

Rapid Urease CLO test is done on biopsy material obtained by gastroduodenoscopy. It is relatively cheap, quick to perform, reasonably specific and sensitive i.e., upto 75-90%^{2,3,10-13}. It however, becomes rather unreliable after antimicrobial therapy and is dependent on gastroduodenoscopy¹⁴.

A microbial culture can be done on biopsy material obtained through gastroduodenoscopy. This is most specific, gold standard and confirmatory but it is not all that easy and also depends on an invasive procedure. It is expensive, time consuming, not universally available and yet provides additional valuable information on antibiotic sensitivity^{2,3,7,8,10}. It has a low sensitivity and a low yield⁷. The organism is fastidious and its culture laborious².

Histology and special stains for *H. pylori* are carried out on biopsy material retrieved by gastroduodenoscopy. It depends on an invasive procedure, is rather expensive, requires technical expertise and takes time to provide results^{2,6,10,15}.

Urea Breath test (UBT) is carried out on subjects using ¹⁴C radioactive or ¹³C non-radioactive material. It is rapid, specific, sensitive and can be helpful in identifying a recent infection. It is expensive and has a significant false negativity^{3,16,17}. Urea Breath Test has a specificity and sensitivity of 90—100%¹⁶. It is not universally available and treatment with proton pump inhibitors (PPI) or antibacterial can give false negative results¹⁷. It is dependent on radioactive material with its associated biohazard and requires expensive equipment for analysis/interpretation.

Qualitative and quantitative detection of antibodies in patient's serum against *H. pylori*, is also increasingly being used. This CLO antibody (IgG) test is simple, quick,

non-invasive, cheap and highly specific (sensitivity upto 95%)^{3,12}. The reliability of this test is questionable in patients over 65 years of age¹⁸, it lacks validation and is subjected to inter-observer variation¹⁹. The antibody titre does not fall for 4-6 months, even after a complete and successful *H. pylori* eradication. Saliva can also be used for this test, but is relatively less sensitive²⁰.

This study was carried out to determine the sensitivity, specificity and predictive values of qualitative CLO antibody test in patients with upper gastrointestinal symptoms so that the test may be used as an effective bedside/outpatient screening test in patients of upper gastrointestinal symptoms to decide who might need an endoscopic evaluation.

Patients, Methods and Results

Thirty seven consecutive patients, in the age group of 15-65 years, presenting with upper

gastrointestinal symptoms (like dyspepsia, pain, nocturnal pain, vomiting, hematemesis) at the PMRC Research Centre, JPMC, Karachi during 1996-1997 were included in the study.

Patients with history of peptic ulcer, surgery for peptic ulcer, recent endoscopy, associated varices, antinulcer therapy, antibacterial therapy, steroid therapy and Immunosuppression were excluded.

Patients were subjected to gastroduodenoscopic evaluation (Olympus GIF 2T20/Fujinon Scope) under topical anaesthesia. Biopsies (one each) were taken from antrum and fundus and CLO urease test carried out by immersing the biopsy material into the prepared gel at 37°C for 30 minutes incubation as described elsewhere²¹ Blood samples (5 till) were taken from each patient and by a qualitative CLO antibody test was done with patients serum using Abbott Flex Pack TM-HP kit, as per manufacturers instructions. Two drops of buffered saline were used as control on the control pad, while one drop of patient's serum was used on test pad and reading was taken at three minutes. Positive test was seen as a distinct red line below the control red line in the test area of the test pad window within three minutes, Eighteen of 37 patients (30 male, 7 female) were less than or equal to 40 years of age and 19 were over 40 years.

Thirty cases had an ulcer (19 anterior small duodenal ulcer, 5 posterior wall duodenal ulcer, 3 multiple duodenal ulcers, 1 duodenal plus gastric ulcer and 1 pre-pyloric gastric ulcer, ulcer). Three ulcers were bleeding, three had associated duodenitis and one had associated esophagitis. Seven cases were non-ulcers: two antral gastritis, one gastritis, one erosive duodenitis, one duodenitis plus gastritis and two cases had normal endoscopy (Tables I and II).

Table I. Correlation of CLO Antibody and CLO Urease.

CLO Antibody	Positive CLO (Urease) by Endoscopy	Negative CLO (Urease) by Endoscopy	Total
Positive	13	4	17
Negative	8	12	20
Total	21	16	37

Table II. HP Antibody test (sensitivity, specificity and predictive values).

	Sensitivity (%)	Specificity (%)	Positive Predictive value (%)	Negative Predictive value (%)
Male (30 cases)	61	75	79	56
Female (7 cases)	50	67	67	50
Age <40 yrs (18 cases)	64	86	88	60
Age >40 years (19 cases)	60	67	67	60
Ulcers (30 cases)	57	75	67	67
Non-ulcers (7 cases)	71	00	71	00
Total (37 cases)	62	75	76.5	60

Seventeen of 37 were CLO antibody positive, while 13 out of these 17 were urease positive as well leaving only 4 behind as negative. Twenty cases were CLO antibody negative and 12 out of these 20 were urease negative as well. There were 8 cases who were CLO urease positive yet antibody negative. They probably represent a recent infection or less likely may be having an inefficient or defective/suppressed immunological response. The overall sensitivity of CLO antibody assay was 62%, specificity 75%, a positive predictive value 76.5% and a negative predictive value of 60% (Table II).

Comments

Identification and isolation of helicobacter pylori and elucidation of its role in upper gastrointestinal disease process was a real breakthrough in a relatively short time¹⁻⁸. In depth analysis of its microbiology, immunology, epidemiology and pathophysiology has revolutionised our understanding of upper gastrointestinal pathology. It has thus led to innovative advances in their management and prevention²⁻¹¹.

A variety of commercial kits are increasingly made available to test for CLO antibody from serum; although laboratory based ELISA is more reliable, more specific and more sensitive^{3,12,18}. ELISA assay, however, is expensive and time consuming requiring technical expertise and equipment. CLO antibody assay on the other hand is simple, quick, popular and cheaper. The test is however subject to

inter observer variance and its correlation with endoscopic evaluation and compared to other available tests, is not very well documented/validated. As IgG remain elevated for upto 6-8 months after eradication, a pre and post treatment quantitative evaluation is highly desirable³. The other factors which can influence the CLO antibody assays are multiple strains infection, drug resistance, antigenic modulation, recurrent and repeated infection and appearance of mutant strains.

The screening for CLO antibodies in young patients is highly effective in reducing the workload on gastroenterologists, screening out the patients who should/should not be subjected to endoscopic examination in busy outpatients/clinics in our setting²². This is particularly important in H. Pylori associated ulcer, gastritis, non-ulcer dyspepsia (NUD) and GI symptoms due to non-organic etiology. It will reduce workload, cut down the expenditure, save valuable time and energy, avoid each and every one to be subjected to endoscopy. A quantitative CLO antibody screening test will probably become a routine clinical protocol before an endoscopy, due to cost effectiveness and reducing the clinical workload. Lastly it is highly useful in sero-epidemiological studies of upper gastrointestinal diseases.

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