EXCELLENT PUBLISHERS

International Journal of Current Research and Academic Review

ISSN: 2347-3215 Volume 3 Number 5 (May-2015) pp. 403-408

www.ijcrar.com

Value of IgG Avidity index for the diagnosis of *Helicobacter pylori* infection

Naser Hajavi, Masoud Shirmohammadi*, Mohammad Reza Bonyady, Morteza Ghojazadeh, Mohammad Hosein Somi

Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences, Imam Reza hospital, East Azerbaijan, Iran

Corresponding author

KEYWORDS

Helicobacter pylori,
Avidity index,
Diagnostic tools

A B S T R A C T

Infection with *Helicobacter pylori* is very common worldwide. Several non-invasive diagnostic tools are available, mostly limited by use of medications by patients. This study aimed to evaluate efficacy of avidity index for diagnosing the infection during medical treatment. The study sample included patients referred to a gastroenterologist in university clinic of Tabriz University of medical sciences without alarm signs. Sensitivity, specificity and the best cut-off value, positive and negative predictive values for this cut-off are reported for IgG avidity compared to results of stool antigen test. From the total of 200 patients, fifty fulfilled the criteria (mean age was 31.12(7.7) years and 62% were females). Serology was positive in 45 (90.0%) patients. Area under the curve was reported to be 0.753, with standard error=0.078 and 95% confidence interval from 0.600 to 0.907 (p=0.006). The best cut-off for IgG avidity was 82.50. At this level the sensitivity was 0.80 and specificity was 0.74. The positive predictive value for this value will be 75.5% and the negative predictive value will be 78.7%. This pilot study evaluated diagnostic efficacy of *H. pylori* IgG avidity compared to results of stool Ag testing and found a good sensitivity and specificity. Clinicians could validate result of a negative stool Ag in more than 70% of patients who can't stop using PPIs or antibiotics.

Introduction

Regardless of the wide variation of *Helicobacter pylori* (*H. pylori*) by geographic area and population groups, it is quite common worldwide (1). The bacterium is mainly acquired through oral ingestion during childhood (2) and becomes chronic during adulthood because it will not cure spontaneously and without treatment (3).

Without treatment, clinical sequels of gastritis due to *H. pylori* could be duodenal or gastric ulcers, mucosal atrophy, gastric carcinoma or gastric lymphoma correlated with the pattern and distribution of gastritis (4). Eradication of *H. pylori* infection is important as gastritis due to *H. pylori* is believed to be a major factor in causing

peptic ulcer disease, especially duodenal ulcers. The majority of patients with gastric ulcers and duodenal ulcers are infected with *H. pylori* (5) and the temporal relationship between development and recurrence of duodenal ulcers with *H. pylori* infection is established in cohort studies (6-7). Eradication of H pylori infection is also recommended in first degree relatives of patients with gastric cancer since this has the potential to reduce the risk of gastric cancer development(8).

There are different endoscopic and noninvasive diagnostic tools with certain advantages and drawbacks for each. Both urea test or antral-biopsy specimen are the first choices when endoscopy is clinically indicated. With the sensitivity of 79-100 and specificity of 92-100 percent, the results may be influenced by taking antibiotics or antoisecretory agents. This may be solved by culture of *H. pylori* with anti-biotic sensitivity testing which is not routinely performed and only suggested for the cases of second line failure(9).

The most common used non-invasive test is the urea breath test (UBT) and has a sensitivity and specificity of more than 90 percent for detecting active infection. However taking proton pump inhibitors (PPIs) and antibiotic drugs may result in false negative results in a considerable percentage of the patients (10). As an alternative, stool antigen test has a high sensitivity and specificity for detecting *H. pylori* infection and are suitable for follow up after an eight week interval (11-13). The result may also be confounded by use of medications (9). The available serology tests detect IgG which is not suitable for detecting active infection as it remains elevated despite decreases of the bacterial load even for years after the eradication of H pylori (14).

The main challenge affecting value of non-invasive diagnostic tools may be the use of medications by patients as described above. A noninvasive method which is not influenced by medications will have great value in clinical practice. IgG avidity assay is a useful method for diagnosis of recent infection and is successfully used for detection of acquired toxoplasmosis (15). The method is based on the amount of functional affinity of specific IgG antibodies which is initially low after infection and increases subsequently in weeks and months. Very little investigations have been established about efficacy of this method for detecting recent *H. pylori* infection. This study aimed to compare efficacy of IgG avidity assay with stool antigen test at active helicobacter infection.

Materials and Methods

This study was conducted in Imam Reza hospital, Tabriz University of medical sciences. The study protocol was approved by the institutional review board of Tabriz University of medical sciences in accordance with the principles of the Declaration of Helsinki.

All consecutive patients referred to a gastroenterologist in university clinic of Tabriz University of medical sciences were eligible. Patients aged 55 or more or with alarm signs (weight loss, vomiting, dysphagia, abdominal mass, anemia, and treatment resistant dyspepsia) were excluded and were referred for endoscopy. Use of PPIs or antibiotics in recent 4 weeks, history of surgery on stomach or duodenum, autoimmune disorders, use of immune suppressive agents and cancer treatment protocols, positive family history or bleeding (16) and congenital or acquired deficits in secretion of antibodies led to exclusion as well.

The procedure was explained for selected patients and all gave written consent. A blood sample was obtained for measuring *H. pylori* IgG antibody and IgG avidity (IDEAL Tashkhis, Iran) and a stool sample was obtained for stool antigen tests (,).

Results are described as mean (standard deviation) or number (percentage) was appropriate. Sensitivity, specificity and the best cut-off value are reported for IgG avidity compared to results of stool antigen test. Receiver Operating Characteristic (ROC) curves were generated to interpret sensitivity and specificity levels and to determine related cut scores. Positive and negative predictive values were calculated for the optimal cut-off compared to results of stool antigen test.

Results and Discussion

From the total of 200 patients, fifty fulfilled the criteria and were included in this study. Their mean age (SD) was 31.12(7.7) years and 62% were females. Main complaints of these patients was pain in 33 patients (66%), bloating in 22(44%) and decreased appetite in 11(22%) patients.

Serology was positive in 45 (90.0%) patients. This included 84.2% of males and 93.5% of females (p=0.285). Five patients with a negative serology were considered non-infected and avidity was not measured consequently.

Result of the test for stool antigen was positive in 30 (60.0%) patients including 63.2% of males and 58.1% of females (p=0.721). all of the patients with a negative serology had a negative result of stool Ag testing.

The ROC curve obtained by plot at different cut-offs for the level of IgG avidity is shown in figure 1. Area under the curve (AUC) was reported to be 0.753, with standard error=0.078 and 95% confidence interval from 0.600 to 0.907 (p=0.006).

When compared to the results of stool Ag testing, the best cut-off for IgG avidity was 82.50. At this level the sensitivity was 0.80 and specificity was 0.74. The positive predictive value for this value will be 75.5% and the negative predictive value will be 78.7%. A lower value of IgG avidity gives a lower sensitivity but a higher specificity. For example, the cut-off of 70 for IgG avidity has the sensitivity of 0.56 and specificity of 0.87.

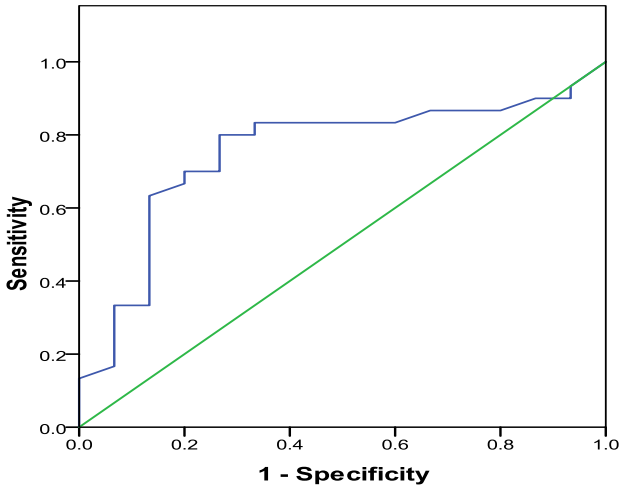
Testing for *H. pylori* is considered in a number of clinical situations. European Helicobacter Study Group recommends the test-and-treat strategy for patients with dyspepsia and without ‘alarm’ symptoms or signs to achieve a significant symptom benefit (8). UBT and stool antigen testing are acceptable non-invasive tests in this setting. The value of these diagnostic tools is vague when medications are used by patients. Some of PPIs and antibiotics are generic drugs and even over-the-counter medications, making them generally available. They are also effective and frequently used for symptomatic treatment of dyspepsia (17). There is a good chance of using PPIs for most of the patients who initial symptom control was insufficient and advanced investigation and treatment in required (18). There should be a washout period for further evaluations diagnostic tests (9) though no study has evaluated the necessary delay after long-term PPIs treatment or antibiotics.

Changes in the IgG affinity during time after primary infection give the opportunity to identify acute vs. chronic infection. The avidity result is determined by using the

ratios of antibody titration curves of urea-treated (which dissociates the antibody-antigen complex) and -untreated sample. When applied for *H. pylori* antibody, the avidity result will be independent from the decreased gastric bacterial load after the use of antimicrobial agents (19).

The current study aimed to benefit from this point in clinical practice. When compared to results of stool Ag testing, IgG avidity lower than 82.50 have a sensitivity of 0.80 and specificity of 0.74 for detecting current infection with *H. pylori*. Results of this study could be interpreted in another way which is more close to clinical practice as well, where the patients can't stop taking PPIs for weeks. Considering the fact that a low IgG avidity indicates recent infection, when stool Ag is negative, a low IgG avidity will verify recent infection and means that the result is not a "false negative" influenced by use of PPIs or antibiotics. Therefore, measuring IgG avidity can validate result of a negative stool Ag in more than 70% of cases. As described within results, a higher specificity is achievable with a lower level of avidity.

Figure.1 ROC curve of IgG avidity for Helicobacter infection diagnosis



H. pylori IgG avidity has not been studied after the study by Basso et al.(20). *H. pylori* IgG avidity had a fair diagnostic value compared to stool AG testing. However, the current study is not introducing the method as an alternative to current well-established tools, but the results could be of certain clinical assistance. When combined with the standard of care, this method could resolve the challenging situation of patients using PPIs or antibiotics. This non-invasive and inexpensive method could validate a negative result of stool AG and ban further evaluations or avoidable treatments.

This study had limitations. Study sample is selected form a population with a high prevalence of *H. pylori* infection (21) and results may not be applicable for low or moderate rate populations. As a pilot study, method is closer to clinical practice for patients without indication for endoscopy. Consequently diagnostic value of avidity test was compared to results of stool Ag testing, which has a high sensitivity and specificity itself (22). However further studies may use the gold standard of invasive tools. Though both stool Ag and avidity testing are in-expensive, cost-

effectiveness of testing both is not evaluated.

In conclusion**,** this pilot study evaluated diagnostic efficacy of *H. pylori* IgG avidity compared to results of stool Ag testing and found a good sensitivity and specificity. Clinicians could validate result of a negative stool Ag in more than 70% of patients who can't stop using PPIs or antibiotics.

Acknowledgments

This study was supported by Liver and gastrointestinal diseases research center, Tabriz University of medical sciences.

References

1.Brown LM. *Helicobacter pylori*: Epidemiology and Routes of Transmission. Epidemiologic Reviews 2000 Jan 1;22(2):283-97.

2.Rowland M, Kumar D, Daly L, O'connor P, Vaughan D, Drumm B. Low rates of *Helicobacter pylori* reinfection in children. Gastroenterology 1999 Aug;117(2):336-41.

3.Walsh JH, Peterson WL. The Treatment of *Helicobacter pylori* Infection in the Management of Peptic Ulcer Disease. N Engl J Med 1995 Oct 12;333(15):984-91.

4.Suerbaum S, Michetti P. *Helicobacter pylori* infection .N Engl J Med 2002 Oct 10;347(15):1175-86.

5.Graham DY. I. *Helicobacter pylori*: Its epidemiology and its role in duodenal ulcer disease. Journal of Gastroenterology and Hepatology 1991 Apr 1;6(2):105-13.

6.Sipponen P, Seppälä K, Aärynen M, Helske T, Kettunen P. Chronic gastritis and gastroduodenal ulcer: a case control study on risk of coexisting duodenal or gastric ulcer in patients with gastritis. Gut 1989 Jul 1;30(7):922-9.

7.Hentschel E, Brandstatter G, Dragosics B, Hirschl AM, Nemec H ,Schutze K, et al. Effect of Ranitidine and Amoxicillin plus Metronidazole on the Eradication of *Helicobacter pylori* and the Recurrence of Duodenal Ulcer. N Engl J Med 1993 Feb 4;328(5):308-12.

8.Malfertheiner P, Megraud F, O'Morain CA, Atherton J, Axon ATR, Bazzoli F, et al. Management of *Helicobacter pylori* infectionGÇöthe Maastricht IV/ Florence Consensus Report. Gut 2012 May 1;61(5):646-64.

9.Malfertheiner P, Megraud F, OGÇÖ Morain C, Bazzoli F, El-Omar E, Graham D, et al. Current concepts in the management of *Helicobacter pylori* infection: the Maastricht III Consensus Report. Gut 2007 Jun 1;56(6):772-81.

10.Gisbert JP, Pajares JM. 13C-urea breath test in the management of Helicobacterpylori infection. Dig Liver Dis 2005 Dec;37(12):899-906.

11.Manes G, Balzano A, Iaquinto G, Ricci C, Piccirillo MM, Giardullo N, et al. Accuracy of the stool antigen test in the diagnosis of *Helicobacter pylori* infection before treatment and in patients on omeprazole therapy. Aliment Pharmacol Ther 2001 Jan;15(1):73-9.

12.Forne M, Dominguez J, Fernandez-Banares F, Lite J, Esteve M, Gali N, et al. Accuracy of an enzyme immunoassay for the detection of *Helicobacter pylori* in stool specimens in the diagnosis of infection and posttreatment check-up. Am J Gastroenterol 2000 Sep;95(9):2200-5.

13.Islam S, Weilert F, Babington R, Dickson G, Smith AC. Stool antigen testing for the diagnosis and confirmation of eradication of *Helicobacter pylori* infection: a prospective blinded trial Intern Med J. 2005 Sep;35(9):526-9.

14.Ekstrom AM, Held M, Hansson LE, Engstrand L, Nyron O. *Helicobacter pylori* in gastric cancer established by CagA immunoblot as a marker of past infection. Gastroenterology 2001;121(4):784-91.

15.Hedman K, Lappalainen M, Seppäiä I, Mäkelä O.. Recent Primary Toxoplasma Infection Indicated by a Low Avidity of Specific IgG. Journal of Infectious Diseases 1989 Apr 1;159(4):736-40.

16.Lin HJ, Lo WC, Perng CL, Li AF-Y, Tseng GY, Sun IC, et al. *Helicobacter pylori* stool antigen test in patients with bleeding peptic ulcers. Helicobacter 2004 Dec 1;9(6):663-8.

17.Talley NJ, Vakil N. Guidelines for the Management of Dyspepsia. Am J Gastroenterol 2005 Oct;100(10):2324-37.

18.Armstrong D, Veldhuyzen van Zanten SJ, Barkun AN, Chiba N, Thomson AB, Smyth S, Sinclair P, et al. Heartburn-dominant, uninvestigated dyspepsia: a comparison of 'PPI-start' and 'H2-RA-start' management strategies in primary care--the CADET-HR Study. Aliment Pharmacol Ther. 2005 May 15;21(10):1189-202.

19.Megraud F, Lehours P. *Helicobacter pylori* Detection and Antimicrobial Susceptibility Testing. Clinical Microbiology Reviews 2007 Apr 1;20(2):280-322.

20.Basso D, Brigato L, Di MF, Plebani M. *Helicobacter pylori* infection and serum IgG avidity. Clin Chim Acta 1996 Feb 9;245(1):129-32.

21.Khedmat H, Karbasi-Afshar R, Agah S, Taheri S. *Helicobacter pylori* Infection in the general population: A Middle Eastern perspective. Caspian J Intern Med 2013;4(4):745-53.

22.Malfertheiner P, Megraud F, OGÇÖ Morain C, Bazzoli F, El-Omar E, Graham D, et al. Current concepts in the management of *Helicobacter pylori* infection: the Maastricht III Consensus Report. Gut 2007 Jun 1;56(6):772-81.