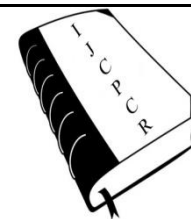




International Journal of Current Pharmaceutical & Clinical Research



www.ijcpcr.com

IMPACT OF PROTON PUMP INHIBITORS ON ENZYME IMMUNOASSAY TESTS FOR HELICOBACTER PYLORI: A COMPARATIVE STUDY WITH STOOL ANTIGEN AND BREATH UREA TESTS

Dr Manish Ranjan*

Assistant professor, Department of General Medicine, Gouri Devi Institute of Medical Sciences and Hospital, Durgapur, India

ABSTRACT

This study aimed to assess the impact of proton pump inhibitors (PPIs) on enzyme immunoassay tests for *Helicobacter pylori* developed by TestMate. A total of 56 patients underwent stool antigen tests and breath urea tests before and after receiving PPI therapy. Before and after PPI treatment, the stool antigen test showed a sensitivity, specificity, and agreement of 96.2%, 72.4%, and 90.3%, respectively, across all 56 patients. Following PPI therapy, breath urea test (UBT) values decreased from 24.98% to 17.19% in 30 patients treated for 4 weeks, indicating a reduction of 4.75%. Moreover, the stool antigen optical density ratios remained relatively consistent before (2.16 ± 0.21) and after (2.17 ± 0.254) treatment, with similar results observed in patients treated for over 4 weeks (2.00 ± 0.27 before treatment and 0.69 ± 0.29 after treatment). Notably, even in the presence of PPI administration, stool antigen testing demonstrated sensitivity comparable to UBT, underscoring its utility and reliability as a diagnostic tool for *Helicobacter pylori* infection across all cases.

Key words: Stool antigen test, *Helicobacter pylori*, Proton pump inhibitor; Urea breath test.

INTRODUCTION

In addition to being highly sensitive, it is also highly specific for diagnosing *Helicobacter pylori* (*H. pylori*) infection, making it the most valuable non-invasive test for *H. Pylori*. According to the 2005 guidelines for diagnosing and treating *Helicobacter pylori*, this is recommended. In addition to the UBT, stool antigen tests use polyclonal and monoclonal antibodies to detect *H. pylori* [1], similarly sensitive and specific. A stool antigen test has also been recommended by Maastricht III for detecting or eliminating *H. pylori* [2]. *Helicobacter pylori* produces catalase as an antigen [3]. Monoclonal antibodies are both rapid, taking only 70 minutes, and have a greater specificity than polyclonal antibodies [4]. UBT is noninvasive and requires a simple laboratory procedure, but it requires more time and training. Furthermore, some patients, such as children, the handicapped, and the elderly,

may have difficulty undergoing UBT. There is a simpler analytical process, fewer medical staff members are required, and stool antigen tests can be used more easily in the case of patients with reduced activities of daily living, children, and the elderly. A proton pump inhibitor (PPI) inhibits gastric acid production and is antibacterial. The use of UBT for *H. Pylori* may provide false-negative results in patients taking PPIs, so PPI treatment should be suspended for at least 2 weeks before UBT for *H. Pylori*. A stool antigen test that uses native catalase as an antigen consists of the Testmate *pylori* antigen enzyme immunoassay (EIA). PPI treatment should not affect the test's accuracy in diagnosing *Helicobacter pylori* infection. A comparison was conducted between stool antigen and UBT post-PPI to determine their comparative accuracy.

Corresponding Author: - Dr Manish Ranjan

METHODOLOGY

56 patients suffering from ulcerative colitis, reflux esophagitis, or other diseases requiring PPIs were evaluated. During and after PPI administration, UBT and stool antigen tests were performed. Subjects were asked to take a breath sample before and after taking a 100 mg UBT tablet®. The CO₂/CO₂ ratio was analyzed by INIS at a cut-off point of 3.5 in order to calculate the CO₂/CO₂ ratio. Each patient's stools were collected prior to and following PPI use, then stored at -80 °C until ready to be used for analysis. Testmate pylori antigen EIA was used for stool antigen testing. At 25°C, 50 mL of 100 mg stool, containing anti-catalase monoclonal antibody conjugated with peroxidase, was added to a well. At wavelengths of 450 and 630 nm, absorbance was measured.

RESULTS

There were 40 positive results for 56 patients after PPI administration, and five negative results for five patients prior to UBT and stool antigen testing. There was one patient who was positive for both stool antigen and UBT tests, while two others were negative. Based on UBT, stool antigen tests had 96.2% sensitivity, 72.4% specificity, and 90.3% agreement before PPI treatment (Table 1).

Following PPI administration, 32 patients reported positive UBT and stool antigen results, and 18 showed negative results. On one patient, the UBT was positive and there was no stool antigen; on two patients, the UBT was positive and the stool antigen test was negative. According to UBT, stool antigen test sensitivity, specificity, and agreement were 89.9%, 91.9%, and 90.3% after PPI treatment (Table 2).

UBT and stool antigen results before and after PPI treatment

Before and after PPI treatment, 76.0% of UBTs were positive. 79.6% of stool antigen tests were positive before and 61.7% were positive after PPI treatment. Prior to or after PPI treatment, the positivity ratios did not differ significantly.

Before and after PPI treatment, UBT and stool antigen values (A values) were measured

UBT values were 24, 98% ± 6.33% before and 17, 19% ± 5.75 % after PPI treatment in 30 patients treated for 4 weeks with PPIs. As a result, the A ratios were 2.16 ± 0.20 before and 1.17 ± 0.24 after PPI treatment. The mean A ratios were also 1.02 ± 0.26 and 0.69 ± 0.28, respectively, for 30 patients treated with PPI for four weeks.

Table 1 : Test results related to proton pump inhibitors including urea breath test results and stool antigen test results

	Urea breath test		Total
	Positive	Negative	
Stool antigen test			
Positive	40	4	44
Negative	2	10	12
Total	42	14	56

Table 2: The results of the urea breath test and stool antigen test in association with proton pump inhibitors

	Urea breath test		
	Positive	Negative	Total
Stool antigen test Positive Negative	32	2	34
Total	4	18	22
	36	20	56

Table 3: Positive rates before and after treatment with proton pump inhibitors

	Before PPI treatment	After PPI treatment	P value
Urea breath test	76.0%	65.3%	0.56
Stool antigen test	79.6%	61.7%	0.16

DISCUSSION

Stool antigen tests are non-invasive tests for Helicobacter pylori, similar to UBTs. With good sensitivity and specificity, this test is simple and easy to perform [8]. In terms of sensitivity, specificity, positive predictive value, and negative predictive value, they were 91%, 93%, 92%, and 87%, respectively, without H. pylori elimination therapy. There were eight reports of monoclonal antibody

tests that had significantly higher sensitivity, specificity, positive predictive value, and negative predictive value. The mean values were 96%, 97%, 96%, and 97%, respectively. As reliable as a UBT, stool antigen tests are also recommended, according to Maastricht III guidelines [2]. Several drugs cause false-negative UBT results, including those that inhibit Helicobacter species, or those that inhibit urease activity [5, 6, 9-12]. False-negative rates

for UBT were 50% in two-week and four-week studies with omeprazole or lansoprazole. One patient treated with 30 mg/d lansoprazole for two weeks had false-negative UBT results. False-negative stool antigen test results are also more common in PPI patients [13, 14]. The UBT result for nine H. Pylori-positive patients receiving PPI was lower. According to the authors, stool antigen tests before PPI treatment showed high sensitivity, but low specificity. With so few patients having negative results on UBT, this may be the reason. In the same vein, despite many reports showing stool antigen tests are highly sensitive and specific, the specificity of these tests has been reported to be lower. In spite of a slight decline in sensitivity after PPI administration, the stool antigen test remained highly specific (90.9%). There was a high degree of concordance (89.3%) between the results before and after PPI administration of UBT and stool antigen tests. Despite taking PPIs before and after taking the test, the stool antigen test performed well. In spite of the fact that stool antigens are highly sensitive and specific, UBT and stool antigen tests differ [16]. By contrast, increasing the stool antigen cut-off resulted in fewer conflicting results. There was a discrepancy between the UBT's inability to detect coccoid H. pylori and its low cutoff score. It is likely that positive stool antigen results and negative results from the UBT are caused by the same mechanism.

The antigen test for Helicobacter Pylori is not significantly different from the UBT in terms of positive rates before and after PPI therapy, suggesting it is an effective test for diagnosing Helicobacter Pylori.

REFERENCE

1. Gisbert JP, Pajares JM. *et al.*, Review article: 13C-urea breath test in the diagnosis of Helicobacter pylori infection -- a critical review. *Aliment Pharmacol Ther.* 20, 2004, 1001-1017
2. Malfertheiner P, Megraud F, O'Morain C, Bazzoli F, El- Omar E, Graham D, Hunt R, Rokkas T, Vakil N, Kuipers EJ. *et al.*, Current concepts in the management of Helicobacter pylori infection: the Maastricht III Consensus Report. *Gut.* 56, 2007, 772-781
3. Gisbert JP, Pajares JM. *et al.*, Stool antigen test for the diagnosis of Helicobacter pylori infection: a systematic review. *Helico- bacter* 2004, 9, 347-368
4. Suzuki N, Wakasugi M, Nakaya S, Kokubo N, Sato M, Kajiyama H, Takahashi R, Hirata H, Ezure Y, Fukuda Y, Shimoyama T. *et al.*, Catalase, a specific antigen in the feces of human subjects infected with Helicobacter pylori. *Clin Diagn Lab Immunol* 9, 2002, 784-788
5. Laine L, Estrada R, Trujillo M, Knigge K, Fennerty MB. *et al.*, Effect of proton-pump inhibitor therapy on diagnostic testing for Helicobacter pylori. *Ann Intern Med.* 129, 1998, 547-550
6. Murakami K, Sato R, Okimoto T, Watanabe K, Nasu M, Fujioka T, Kodama M, Kagawa J. *et al.*, Influence of anti-ulcer drugs used in Japan on the result of (13)C-urea breath test for the diagnosis of Helicobacter pylori infection. *J Gastroenterol* 38, 2003, 937-941
7. Suzuki N, Wakasugi M, Nakaya S, Okada K, Mochida R, Sato M, Kajiyama H, Takahashi R, Hirata H, Ezure Y, Koga Y, Fukuda Y, Shimoyama T. *et al.*, Production and application of new monoclonal antibodies specific for a fecal Helicobacter pylori antigen. *Clin Diagn Lab Immunol* 9, 2002, 75-78
8. Malfertheiner P, Mégraud F, O'Morain C, Hungin AP, Jones R, Axon A, Graham DY, Tytgat G. *et al.*, Current concepts in the management of Helicobacter pylori infection--the Maastricht 2-2000 Consensus Report. *Aliment Pharmacol Ther* 2002, 16, 167-180
9. Chey WD, Woods M, Scheiman JM, Nostrant TT, DelValle J. *et al.*, Lansoprazole and ranitidine affect the accuracy of the 14C- urea breath test by a pH-dependent mechanism. *Am J Gas- troenterol.* 92, 1997, 446-450

Compared to UBT, stool antigen positivity fell by 78.6% to 60.7% after PPIs were administered. Stool antigen tests are as useful as UBTs without discontinuation of PPIs. Neither stool antigen testing nor UBT results were significantly different. Patients treated with PPI for 4 weeks had significantly lower UBT results, but not stool antigen results. Both assays were affected by PPIs' bacteriostatic effects, but UBT was less affected by PPIs' bacteriostatic effects as compared with stool antigen. PPIs maintained stool antigen results more consistently despite several studies reporting false-negative results during PPI treatment. As a non-invasive test for Helicobacter pylori, stool antigen has several advantages over the UBT, including ease, rapidity, and low cost [17]. In addition to its high sensitivity and specificity, stool antigen testing is also fast and easy [18]. Whenever UBTs are not available, stool antigen tests should be used for diagnosis.

CONCLUSION

Worldwide, the number of patients receiving PPI therapy is increasing, and many patients, such as the elderly and those with limited activities of daily living, have difficulty undergoing UBT. In these patients, stool antigen tests are reliable and useful. Stool antigen test results remained stable during PPI treatment, and were comparable to UBT results. Results of the stool antigen test were more stable when patients were taking PPI for four weeks. For this reason, stool antigen tests are useful and reliable for diagnosing Helicobacter pylori.

10. Connor SJ, Seow F, Ngu MC, Katelaris PH. *et al.*, The effect of dosing with omeprazole on the accuracy of the 13C-urea breath test in Helicobacter pylori-infected subjects. *Aliment Pharmacol Ther.* 13, 1999, 1287-1293
11. Savarino V, Bisso G, Pivari M, Zentilin P, Bilardi C, Dul-becco P, Mele MR, Tracci D, Vigneri S. *et al.*, Effect of gastric acid suppression on 13C-urea breath test: comparison of ranitidine with omeprazole. *Aliment Pharmacol Ther* 2000; 14: 291-297
12. Adachi K, Fujishiro H, Mihara T, Komazawa Y, Kinoshita Y. *et al.*, Influence of lansoprazole, famotidine, roxatidine and rebamipide administration on the urea breath test for the diagnosis of Helicobacter pylori infection. *J Gastroenterol Hepatol* 2003, 18, 168-171
13. Manes G, Balzano A, Iaquinto G, Ricci C, Piccirillo MM, Giardullo N, Todisco A, Lioniello M, Vaira D. *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* 15, 2001, 73-79
14. Bravo LE, Realpe JL, Campo C, Mera R, Correa P. *et al.*, Effects of acid suppression and bismuth medications on the performance of diagnostic tests for Helicobacter pylori infection. *Am J Gastroenterol* 94,1999, 2380-2383
15. Fukuda Y, Tomita T, Kosaka T, Hori K. *et al.*, [Evaluation of diagnostic methods for Helicobacter pylori infection]. *Nihon Rinsho* 62, 2004, 459-463
16. Masoero G, Lombardo L, Della Monica P, Vicari S, Crocilla C, Duglio A, Pera A. *et al.*, Discrepancy between Helicobacter pylori stool antigen assay and urea breath test in the detection of Helicobacter pylori infection. *Dig Liver Dis* 32, 2000, 285-290
17. Manes G, Zanetti MV, Piccirillo MM, Lombardi G, Balzano A, Pieramico O. *et al.*, Accuracy of a new monoclonal stool antigen test in post-eradication assessment of Helicobacter pylori infection: comparison with the polyclonal stool antigen test and urea breath test. *Dig Liver Dis* 37, 2005, 751-755
18. Kato S, Ozawa K, Okuda M, Nakayama Y, Yoshimura N, Konno M, Minoura T, Iinuma K. *et al.*, Multicenter comparison of rapid lateral flow stool antigen immunoassay and stool antigen enzyme immunoassay for the diagnosis of Helicobacter pylori infection in children. *Helicobacter* 9, 2004, 669-673