

Original article

Prevalence of Helicobacter Pylori in symptomatic patients post triple therapy eradication in Jordan

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Abstract

Background and Objective: Despite the use of triple therapy for H.pylori eradication, significant number of the patients still has same complaint. In view of their complaint and increase number of the studies showed decrease in the cure rate of triple therapy, we look at the prevalence of Helicobacter Pylori (HP) in symptomatic patients post a fourteen days' course of triple therapy in documented HP gastritis by histopathology.

Method and Materials: A retrospective study, which includes one hundred and five patients, whom underwent endoscopies for epigastric pain, from May 2014 till February 2015, and have had gastric biopsies that showed chronic active gastritis with presence of HP. Triple eradication therapy in the form of omeprazole 20mg BID, amoxicillin 1g BID and clarithromycin 500mg BID was given for 14 days. These patients were selected as they remain symptomatic post eradication therapy. The presence of HP after eradication was confirmed by stool antigen test six weeks after the end of treatment with complete avoidance of antibiotics, proton pump inhibitors and histamine 2 receptor antagonists during this period.

Result: The rate of eradication in these symptomatic patients was 61.9%. Failure of eradication was seen in 33.3% of the male group (10 patients) and 40% of the female group (30 patients).

Conclusion: Our study showed that triple therapy eradication rate was 61.9%, which is lower than international findings; this may be explained by fact that we only screened the symptomatic patient post eradication therapy and not all patients who received the course. Studies on HP sensitivity for antibiotic should be done to guide eradication regimens to reach acceptable eradication rates.

Key Words: *Helicobacter Pylori, Triple therapy, Gastritis, Stool Antigen test*

Introduction

Helicobacter Pylori (HP) is a gram negative microaerophilic bacteria that colonize gastric mucosa. It causes chronic inflammation in all infected patients, but it is clinically apparent in only 10-20%. The clinical presentation varies; acute and chronic gastritis, atrophic gastritis, metaplasia, gastric lymphoma and gastric adenocarcinoma. (6, 7, 8)

Worldwide, the prevalence of HP infection increases with age reaching 40-60% in asymptomatic elderly persons. (6, 7, 8)

Several diagnostic methods are used in detection of HP; these are divided into invasive and noninvasive.

Noninvasive methods include urea breath test (sensitivity and specificity 95% and 91% respectively), stool antigen test (sensitivity and specificity 91.6% and 98.4% respectively) and serology (sensitivity and specificity 85% and 79% respectively). (6)

Invasive methods for diagnosis include histopathology, which is considered the gold standard for diagnosis, rapid urease test (sensitivity

of 96% and specificity of 90%) and culture (sensitivity of 90% and specificity of 100%).

Confirmation of eradication is usually done 4-6 weeks after end of treatment by urea breath test or stool antigen test.

Indication for treatment of HP include peptic ulcer disease, nonulcer dyspepsia, atrophic gastritis, post gastric cancer resection, first degree relative for patient with gastric cancer, gastric MALT lymphoma, any patient on long-term NSAID with history of upper gastrointestinal bleeding or ulcer, unexplained iron deficiency anemia, Idiopathic thrombocytopenic purpura and lastly patient's wishes.(6)

First line of treatment for HP which is the triple therapy which consists of PPI twice daily, clarithromycin 500mg BID and amoxicillin 1g BID for 7 to 14 days. If this fails sequential, concomitant, sequential-concomitant or bismuth quadruple therapy can be tried. If any one of these failed then tailored therapy and lastly salvage therapy can be tried.

Antibiotic resistance is considered the most important factor for failure of triple eradication therapy, mainly resistance to Clarithromycin. It has become unacceptable to give triple therapy in areas where the prevalence of Clarithromycin resistance 10-20% or more.

Method

From May 2014 till February 2015, one hundred and five patients whom underwent upper endoscopy for epigastric pain and had documented HP chronic active gastritis by histopathology with no response to triple eradication therapy were sent to confirm the eradication by stool antigen test.

This retrospective study was done at the endoscopy unit in King Hussein Medical Hospital.

All patients received fourteen days course of omeprazole 20mg BID, clarithromycin 500mg BID and amoxicillin 1g BID. Then, the eradication was confirmed six weeks after the end of the eradication therapy. The avoidance of PPI and antibiotics in this time interval was confirmed.

Result

One hundred five patients underwent stool antigen test as they remain symptomatic post triple therapy. The age of the patients ranged from sixteen years to sixty years with mean age of twenty eight. 71.4% of these patients (75 patients) were females and 28.6% (30 patients) were males. 40 out of 105 patients (38.1%) were stool antigen test positive and 65 patients (61.9%) were negative. In the male group 10 out of 30 patients were positive (33.3%), whereas in female group it was 30 out of 75 patients were positive 40%. (See table 1, 2)

Discussion

Our study was aimed to assess the cure rate of triple therapy eradication, as there is growing evidence of decrease rate of HP eradication with triple therapy and shifting to other regimens as a first line eradication therapy.

A review article published in 2011 in *Alimentary Pharmacology & therapeutics* by J. P. Gisbert et al, entitled "The Effectiveness of Standard Triple Therapy for *Helicobacter pylori* Has Not Changed Over the Last Decade, But it is Not Good Enough". They analyzed 32 studies done in Spain which include 4727 patients showed a mean 80% cure rate, and by analysis of 13 studies which included 3293 patients showed that mean resistance for clarithromycin was 8%. This review showed that the cure rate from 1997 till 2008 did not change.(3) Despite this review article, multiple studies were done in Spain after that showed lower cure rate. A multicenter clinical trial was done in Spain comparing triple therapy with Hybrid and Concomitant therapy showed that cure rate in Triple therapy was 70% compared to 90.8% and 90% in Hybrid and concomitant therapy, respectively.(10) The lower cure rate was observed in other study, which was done also in Spain, even when the triple therapy optimized by the use of Esomeprazole 40mg twice daily compared to optimized concomitant therapy for fourteen days (82.3% Vs 93.8%) favoring optimized concomitant therapy as first line eradication therapy over Triple therapy.(11)

Other study published in *Acta Gastroenterology of Belgium* in Sep 2011 by Karatapanis et al for effective of 7,10 and 14 days rabeprazole-based standard triple therapies for HP eradication done on Greek patients showed that the eradication rates were 74.5% for 7-days, 80.6% for 10-days and 90.2% for 14-days treatment.(2)

A study was done in china and published in August 2010 in the *Journal of Digestive diseases* by Shu Dong Xiao showed that the eradication rate for triple therapy was 65.1% and resistance for clarithromycin was 20.8%. (1)

A Japanese study was published in February 2012 in the *World Journal of Gastroenterology Pharmacology and Therapeutics* By Ayako Yani et al, compared non bismuth quadruple therapy (lansoprazole, amoxicillin, clarithromycin and metronidazole) versus triple therapy for seven days and showed that the eradication rate for this quadruple therapy was 94.9% versus 68.3% in the triple therapy group. (4) Another recent study was done from Asian perspective regarding first line eradication therapy by Miftahussurur M and Yamaoka Y find out that surveillance of antibiotic resistant and patient's prior usage of antibiotic, in addition to use high dose of PPI or non enzymatic

PPI are all essential to combat H.pylori resistance.(9)

In Tunis a prospective randomized study was done on 85 Tunisian patients compared clarithromycin to metronidazole each in a triple therapy regimen, and published in La Tunisie Medicale in January 2012 showed that the eradication rate in the clarithromycin based therapy was 69.9% versus 48.7% in metronidazole based therapy group.(5)

These studies showed that efficacy of triple therapy did not reach 80% in most of them, which reflects increased resistance of HP to clarithromycin and variable prevalence of clarithromycin resistance in different regions .This necessitates the need to assess the resistance of HP to the different antibiotics in order to guide the eradication therapy.

Conclusion
Our study showed that the eradication rate of triple therapy was 61.9% which is below the observed in international studies; this may be explained by the fact that we only evaluated the symptomatic patients post eradication and we did not test all the patients who received the triple therapy. Despite this, the eradication rate is still very low and reflects the need for further studies to assess HP antibiotic resistance patterns to guide our eradication therapy regimen.

References

1. Zheng Q,Chen WJ,LuH,SunQJ,XiaoSD. Comparison of the efficacy of triple versus quadruple therapy on the eradication of Helicobacter pylori and antibiotic resistance.J Dig Dis.21 Oct;11(5):313-8.PMID: 20883428.
2. Karatapanis S, Georgopoulos SD, Papastergiou V, Skorda L, Papantoniou N, Lisgos P,et al. "7, 10 and 14-days rabeprazole-based standard triple therapies for H. pylori eradication: are they still effective? A randomized trial".Acta Gastroenterol Belg. 2011 Sep;74(3):407-12. PMID: 22103045
3. Gisbert JP, Calvet X. Review article: the effectiveness of standard triple therapy for Helicobacter pylori has not changed over the last decade, but it is not good enough. Aliment Pharmacol Ther. 2011 Dec;34(11-12):1255-68. PMID: 2201774.
4. Yanai A, Sakamoto K, Akanuma M, Ogura K, Maeda S. Non-bismuth quadruple therapy for first-line Helicobacter pylori eradication: A randomized study in Japan. World J Gastrointest Pharmacol Ther. 2012 Feb 6;3(1). PMID: 22408744
5. Lohmari H1, Bdioui F, Bouhleb W, Melki W, Hellara O, Ben Chaabane N,et al. Clarithromycin versus metronidazole in first-line Helicobacter pylori eradication. Prospective randomized study of 85 Tunisian adults. Tunis Med. 2012 Jan;90(1):31-5. PMID: 22311445
6. Selgrad M, Kandulski A, Malfertheiner P. Helicobacter pylori: diagnosis and treatment. Curr Opin Gastroenterol. 2009 Nov;25(6):549-56. PMID:19696666.
7. Proença-Modena JL, Acrani GO, Brocchi M. Helicobacter pylori: phenotypes, genotypes and virulence genes. Future Microbiol. 2009 Mar;4(2):223-40. PMID: 19257848.
8. Toyokawa T, Suwaki K, Miyake Y, Nakatsu M, Ando M. Eradication of Helicobacter pylori infection improved gastric mucosal atrophy and prevented progression of intestinal metaplasia, especially in the elderly population: a long-term prospective cohort study. J Gastroenterol Hepatol. 2010 Mar;25(3):544-7. PMID:19817964.
9. Miftahussurur M, Yamaoka Y. Appropriate First-Line Regimens to Combat Helicobacter pylori Antibiotic Resistance: An Asian Perspective. Molecules. 2015 Apr 8;20(4):6068-6092. PMID: 25856059.
10. Cuadrado-Lavín A, Salcines-Caviedes JR, Diaz-Perez A, Carrascosa MF, Ochagavía M ,et al. First-line eradication rates comparing two shortened non-bismuth quadruple regimens against Helicobacter pylori: an open-label, randomized, multicentre clinical trial. J Antimicrob Chemother. 2015 Apr 7. PMID: 25855760.
11. Molina-Infante J, Lucendo AJ, Angueira T, Rodriguez-Tellez M, Perez-Aisa A,et al. Optimised empiric triple and concomitant therapy for Helicobacter pylori eradication in clinical practice: the OPRICON study. Aliment Pharmacol Ther. 2015 Mar;41(6):581-9. PMID: 25776067.