THE EFFICACY OF THE STANDARD TRIPLE ANTI HELICOBACTER PYLORI THERAPY IN ENDOSCOPY-PROVEN DUODENAL AND GASTRIC ULCERS

Mohammad A. Al Sheikhani [a] and Bnar Sardar Saida [b]

Submitted: 12/2/2017; Accepted: 1/8/2017; Published: 15/8/2017

ABSTRACT

Background

Helicobacter pylori infection has a high global prevalence and carries a significant disease burden. For more than 10 years now, the recommended therapy worldwide for eradication has been a standard triple therapy with amoxicillin, clarithromycine and a proton pump inhibitor. The success of this therapy has been declined in the recent years due to many factors.

Objectives

To determine the efficacy of the current standard triple anti-*Helicobacter pylori* treatment in Slemani.

Patients and Methods

This is a prospective study enrolling 62 patients carried out at Shar teaching hospital endoscopy department during a period from January 2015 through January 2016. Patients with gastric and duodenal ulcer underwent biopsy taken from body and antrum of their stomach (one sample from each part), along with stool samples for monoclonal stool antigen testing. They were subjected to standard triple therapy for 2 weeks. After 4 weeks of completion of the treatment they underwent stool antigen test to confirm the eradication.

Results

The eradication rate was 58%. Male gender, smoking, diabetes and non-steroidal anti inflammatory dug use had reduced chance of cure.

Conclusion

The eradication rate was low in our locality for the standard triple therapy. Possibly due to many factors, including rising numbers of antibiotic resistance, smoking, poor compliance and comorbidities like diabetes mellitus.

Keywords: *H.pylori, Triple therapy, Gastric ulcer, Duodenal ulcer.*

[a] Kurdistan Center for Gastrohepatology and Hepatology; Department of Medicine, College of Medicine, University of Sulaimani. Correspondence: shaikhanimohammad@googlemail.com
[b] Shar Hospital, Directory of Health, Ministry of Health, Sulaimani, Iraqi Kurdistan, Iraq.

https://doi.org/10.17656/jsmc.10122

INTRODUCTION

Various consensus groups, including the group at the Maastricht IV consensus meeting, recommended a triple-therapy regimen containing a proton pump inhibitor (PPI), clarithromycin, and either amoxicillin or metronidazole as first-line treatment for the eradication of *H. pylori*. However, recent reports indicate that these regimens achieve only about a 70% eradication rate. The most important cause for the reduced success of standard triple therapy is the increasing rate of *H. pylori* clarithromycin/ metronidazole resistance [(1)].

The effectiveness of the most commonly used therapies has been increasingly compromised by the rapid emergence of antibiotic-resistant strains of *H. pylori* and by poor adherence to treatment by patients. These factors have reduced the effectiveness of treatment to unacceptable levels (≤ 80%) in many geographic areas. Consequently, new treatment strategies have recently been validated and used to replace the standard triple therapy. These approaches have especially been used in areas with a high resistance to clarithromycin, which is a major risk factor for failure of treatment regimens [(2)] .Resistance to amoxicillin has remained relatively stable, while resistance rates to metronidazole and clarithromycin have been steadily increasing [(3-4)]. The prevalence of antibiotic resistance varies considerably by region and is related to the use of antibiotics, such as clarithromycin and metronidazole, for respiratory or gastrointestinal infections, respectively [(5)]. There are several other explanations for why clarithromycin susceptibility reduces the success rate of therapy. These explanations include a poor adherence to the drug regimen by the patient, gastric acidity, concentration of bacterial strains, and bacterial mutations [(6)].

Objective

To determine the efficacy of the current standard triple anti-*Helicobacter pylori* treatment in Slemani.

PATIENTS AND METHODS

This is a prospective study enrolling 62 patients carried out at Shar teaching hospital endoscopy department during a period from January 2015 through January 2016.

Patients with gastric and duodenal ulcer underwent biopsy taken from body and antrum of their stomach (one sample from each part), along with stool samples for monoclonal stool antigen testing. They were subjected to standard triple therapy (Omeprazole 40 mg/ day, Amoxycillin 1 gm twice daily and Clarithromycin 500 mg twice daily) for 2 weeks. After 4 weeks of completion of the treatment they underwent stool antigen test to confirm the eradication. The thesis was approved by the ethical committee at Kurdistan Board for Medical Specialities. The analysis were performed using SPSS 18.0 and significance was set at $p<0.05$.

RESULTS

Sixty-two patients fulfilled the entry criteria, the mean age +/-standard deviation was 38.097±14.83. Fourty-one (66.2%%) of them were male and 21(33.8%) were female, 23 (28.7%) were smokers, NSAID users were four cases, and 11 were alcoholic. The characteristics of the populations is shown in Table 1.

Thirty-six patients (58%) fulfilled the criteria of complete eradication after the standard treatment, the cure rate among the smokers was 39% and 54.5% in alcoholics, while the response rate in NSAID users was 25%. Fifteen out of 21 females (71.4%) were cured after the treatment, and 21 (51.2%) of the 41 male patients showed response to the therapy.

Table 1. Characteristics of the patients entering the analysis with OGD findings.

Parameter	Number
Age (mean +/- std)	(38.09+14.83)
Gender (male/female)	(41/21)
Risk factors	
Smoking	23 (37%)
Alcoholic	11 (17.7%)
NSAID use	4 (6%)
Diagnostic finding	
DU	46 (74%)
GU	12 (19.6%)
DU & GU	4 (6.4%)

Table 2. Relation between gender and the therapy (cross tabulation). p-value 0.1.

Gender	Responding		Not responding		Total	
	No.	%	No.	%	No.	%
Male	21	51.2	20	48.8	41	100
Female	15	71.4	6	28.6	21	100

Table 3. Effect of smoking on the therapy, p-value 0.033.

Habit	Responding		Not responding		Total	
	No.	%	No.	%	No.	%
Smoker	9	39	14	61	23	100
Non-smoker	27	71.4	12	28.6	39	100

Table 4. Effect of alcohol on the response to therapy (cross tabulation). p-value 0.36.

Habit	Responding		Not responding		Total	
	No.	%	No.	%	No.	%
Alcoholic	6	54.5	5	45.5	11	100
Not alcoholic	30	58.8	21	41.2	51	100

Table 5. Endoscopic findings of the patients. P-value 0.5.

OGD finding	Responding		Not responding		Total	
	No.	%	No.	%	No.	%
Duodenal ulcer	24	52.2	22	47.8	46	100
Gastric ulcer	8	58.3	4	41.7	12	100
GU & DU	4	100	0	0	4	100

Table 6. Geographic distribution of the patients, cross tabulation. p-value 0.34.

Geographic distribution	Responding		Not responding		Total	
	No.	%	No.	%	No.	%
Inside city center	29	60.4	19	39.6	48	100
Outside city center	7	50	7	50	14	100

Table 7. comorbidities of the enrolled patients, cross tabulation. p-value 0.242.

Comorbidities	Responding		Not responding		Total	
	No.	%	No.	%	No.	%
DM	6	43.7	9	56.3	15	100
No DM	29	63	17	37	46	100

Table 8. Age as a factor on the response. Independent sample t-test, p-value=0.5.

Response	N	Mean	Std. Deviation	95% Confidence Interval for Mean		Minimum	Maximum
				Lower Bound	Upper Bound		
No	26	38.231	11.6732	33.516	42.946	23.0	70.0
Yes	36	38.000	16.3777	32.459	43.541	12.0	70.0
Total	62	38.097	14.4831	34.419	41.775	12.0	70.0

Table 9. relation between NSAID use and the response to therapy(cross tabulation). p-value 0.3.

NSAID user	Responding		Not responding		Total	
	N	%	N	%	N	%
Yes	1	25	3	75	4	100
No	35	60.3	23	39.7	58	100

DISCUSSION

The eradication rate reached 58% in our study, which is not satisfactory compared to many other centers, but also equals or even higher than some others [7, 8]. The difference could be due to many factors; such as evolving the numbers of antibiotic resistance specially Clarithromycine as in many other places,[9-11] or poor compliance of the drug by the patients probably due to the adverse effects, length and frequency of the therapy, poor education and unawareness about the therapy and the risk of the bacteria.

A published study in September 2014 from Turkey enrolling 43 patients; showed the eradication rate of standard triple therapy to be about 53.4% [9]. In a meta-analysis published in 2014 among around 42000 patients in Korea showed eradication rate of 74.6%. [12] In Spain; the triple therapy is still acceptable as it reaches 82% based on 32 studies (4727 patient) [13].

A ranomised controlled trial done among 488 patients in seven Latin American countries in 2011 showed eradication rate of 82.2% and even higher than the concomitant therapy [14] .In United States, two recent large double-blind, multicentre studies performed in the United States both found eradication rates of 77% with standard therapy [15]. In a retrospective study in Italy which was done on 1497 patients, the efficacy appeared to be around 70% [16]. A recent study done in Saudi Arabia on 103 patients subjected to the standard triple therapy showed eradication rate of 67.6% [17].

Smoking had significant negative effect on the cure rate, as the rate of eradication was 39% in the smokers, possibly due to increased gastric acidity and damage to mucosal protective factor by the smoking [18]. The effect of alcohol drinking had slight effect on the response, in our study the eradication rate was in 7 from 12 alcoholics (54.5%, although the sample size is small), also age of the patients had no role in the response. Females showed higher eradication rate than males in our study (71.4% vs 51.2%), which can be explained by higher number of smoking and consumption of multisource foods among male patients. In a study published in United states in 1993, by Culter et al, showed no effect of patient demographic factors like gender, smoking, alcohol on eradication rate.

A published study in Poland in 2008 among 250 patients showed that smoking lowers the efficacy but alcohol has no effect on it [19].

A result of 22 published studies (5532 patients) in Japan showed the inverse relationship between smoking and *H. pylori* eradication [20]. The response to therapy was higher among patients living in center of the cities compared to outside (60.4% vs 50%) which may be due to poor hygiene, increased use of unprescribed antibiotics in rural areas and good compliance with completion of eradication therapy by the urban people.

The effect of the therapy was also low in diabetics (40%), as has been seen the result of other studies. Possible explanations can be the decreased immunity and antibiotic efficacy due to poor gastric vasculature in diabetics, gastroparesis, in addition to increased use of the antibiotics due to the high affinity to other infections like UTI, diabetic foot ulcer and respiratory infections.

In a study published in 2009 by Demir et al, among 56 diabetic patients versus 58 age-matched control patients, showed higher Clarithromycine resistance and treatment failure rate in diabetics [21]. Another study in 2003 done in Turkey by Mehmet et al, showed eradication rate of 50% in diabetics versus 85% in non-diabetic controls [22]. Other than relation with smoking; the other results of relations to therapy were not significant in our study, the main reason for this is the small sample of the enrolled patients.

Conclusion

The efficacy of the standard triple therapy was low and unsatisfying in our study. The emerging number of Clarithromycin resistance is probably the main reason due to increased prescription of the antibiotic for other indications. Other factors include: poor compliance due to adverse effects and poor knowledge about the disease by the patients. Smoking, male gender, NSAID use, living in rural areas all reduces the rate of successful eradication.

REFERENCES

1. Malfertheiner P, Megraud F, O'Morain CA et al. Management of Helicobacter pylori infection--the Maastricht IV/ Florence Consensus Report. Gut. 2012 May;61(5):646-64.

2. Jafri NS, Hornung CA, Howden CW, et al. Meta-analysis: sequential therapy appears superior to standard therapy for Helicobacter pylori infection in patients naive to treatment. Ann Intern Med . 2008 Jun 17;148(12):923-31. Epub 2008 May 19

3. Mégraud F. Current recommendations for Helicobacter pylori therapies in a world of evolving resistance. Gut Microbes. 2013;4:Epub ahead of print.

4. Thung, H. Aramin, V. Vavinskaya, S. Gupta, J. Y. Park, S. E. Crowe, M. A. et all. Review article: the global emergence of Helicobacter pylori antibiotic resistance;Aliment Pharmacol Ther. 2016 Feb; 43(4): 514–533.

5. Su P, Li Y, Li H, et al. Antibiotic resistance of Helicobacter pylori isolated in the Southeast Coastal Region of China. Helicobacter. 2013;18:274–279.

6. Lee JW, Kim N, Kim JM, et al. Prevalence of primary and secondary antimicrobial resistance of Helicobacter pylori in Korea from 2003 through 2012. Helicobacter. 2013;18:206–214.

7. De Francesco V, Margiotta M, Zullo A, et al. Prevalence of primary clarithromycin resistance in Helicobacter pylori strains over a 15 year period in Italy. J Antimicrob Chemother. 2007;59:783–785.

8. Garza E, Guillermo Ignacio, Héctor Jesús , Francisco Javier. A review of Helicobacter pylori diagnosis, treatment, and methods to detect eradication. World J Gastroenterol. 2014 Feb 14; 20(6): 1438–1449 .

9. Georgopoulos SD, Papastergiou V, Karatapanis S. Current options for the treatment of Helicobacter pylori. Expert Opin Pharmacother. 2013;14:211–223.

10. Alsohaibani F, Alashgar H, Alkahtani K, et al. prospective trial in Saudi Arabia comparing the 14-day standard triple therapy with the 10-day sequential therapy for treatment of Helicobacter pylori infection. Saudi J Gastroenterol 2015;21:220-5

11.Megraud F., Coenen S., Versporten A., et al. Helicobacter pylori resistance to antibiotics in Europe and its relationship to antibiotic consumption. 2011.

12 Eun Jeong Gong, Sung-Cheol Yun, Hwoon-Yong Jung, et al. Meta-Analysis of First-Line Triple Therapy for Helicobacter pylori Eradication in Korea: Is It Time to Change? J Korean Med Sci. 2014 May;29(5):704-713. English

13 Shiota S, Rita Reddy, Abeer Alsarraj,et al. Graham, Antibiotic Resistance of Helicobacter pylori Among Male United States Veterans, September 2015 Volume 13, Issue 9, Pages 1616–1624.

14. Thung. Global emergence of Helicobacter pylori antibiotic resistance. Aliment pharmacol Ther 2016; 43: 514-533.

15. J. P. Gisbert; X. Calvet, 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;34(11):1255-1268.

16. Greenberg ER, Anderson GL, Morgan DR, et al. 14-day triple, 5-day concomitant, and 10-day sequential therapies for Helicobacter pylori infection in seven Latin American sites: a randomised trial. Lancet, 2011 Aug 6;378(9790):507-14.

17. Vakil N, Lanza F, Schwartz H. Seven-day therapy for Helicobacterpylori in the United States. AlimentPharmacol Ther 2004; 20: 99–107.

18. Tursi A, Elisei W, Giorgetti G, et al. Decreasing efficacy of the standard seven-day triple therapy containing amoxycillin and clarithromycin in curing Helicobacter pylori infection in clinical setting in Italy: a 10-year follow-up study. Panminerva Medica [2014, 56(1):57-61]

19. Namiot DB, Leszczynska K, Namiot Z. Smoking and drinking habits are important predictors of Helicobacter pylori Eradication. Advances in Medical Sciences. 2008, 53(2): 310-15.

20. Suzuki T, Matsuo K, Ito H, et al. Smoking increases the treatment failure for Helicobacter pylori eradication. Am J Med. 2006;119:217-224

21. Demir M., Gokturk HS, Ozturk NA et al. Clarithromycine resistance and efficacy of Clarithromycine-containing triple eradication therapy for Helicobacter Pylori infection in type 2 diabetes mellitus patients. Southern Medical Journal 2009;102(11):1116-1120.

22. Sargyn M, Oya Uygur Bairamicli, Haluk Sargin et al. Type 2 diabetes mellitus affects eradication rate Helicobacter pylori. World J Gastroenterol, 2003 May 15; 9(5) 1126-1128.