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Effectiveness of Different Treatment Regimens on Eradication of Helicobacter Pylori Infection (A Single Center Experience in Kuwait)

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Abstract

Background: Helicobacter pylori treatment still remains a challenge for physicians, and no current first-line therapies are able to cure the infection in all treated patients, recent studies reported declining in eradication rate with commonly usedclarithromycin based triple therapy and high cure rate was observed in patients treated by other regimens such as bismuth based therapy.

Aim of the Study : To evaluate the effectiveness of the different regimens (Clarithromycin based triple therapy, bismuth based therapy and levofloxacin based therapy) on eradication of H.pylori infection.

Methods: The data of 510H. pylori-infected treatment-naïve subjects (215 males, 295 female) were collected retrospectively through period between January 2014 and December 2016. Patients treated at Gastroenterology Clinic Al-Sabah Hospital Kuwait. Four hundred and twenty nine patients treated by clarithromycin based triple therapy, 75 patients treated by bismuth containing quadruple therapy. C13 urea breath test was used for confirm eradication.

Results: Eradication rate was significantly higher in 10 days bismuth based quadruple regimen than 14 days clarithromycin based triple regimen (96%, 77% respectively) ($p<0.001$). Levofloxacin based triple therapy and bismuth based quadruple therapy were effective 2nd line therapy (≥90% cure rate).

Conclusion: Bismuth based quadruple regimen more effective therapy for H.pylori infection than clarithromycin based triple regimen. Levofloxacin based triple and bismuth based quadruple regimens are effective 2nd line therapy with high cure rate.

Key Words: *Helicobacter Pylori Infection.*

Introduction

HELICOBACTER pylori is chronic infection of stomach causing chronic gastritis, gastroduodenal ulcers, and gastric cancer, approximately more than 50% of population infected worldwide most of them in developing countries **[1,2]**. Eradication of H. pylori has been recommended for all infected subjects as it is important in treating gastrointestinal diseases and preventing its complications, multiple regimens consist of proton pump inhibitor plus antibiotics combinations have been used for treatment of infected individuals **[3]**. Clarithromycin based triple therapy thought to be one of the most effective regimen for H.pylorieradication. However, with increasing clarithromycin resistance the eradication rate achieved by this regimen has been declining with less than 80% cure rate that consider it as sub-optimal therapy for H.pylori **[4-6]**. Bismuth quadruple therapy is currently recommended as an alternative first-line treatment for H. pylori infection as it provides superior eradication with similar safety and tolerability to standard therapy **[7,8]**. For patients in areas where clarithromycin resistance is high (> 15 percent) bismuth-containing or concomitant non-bismuth containing quadruple therapy should be used as first-line therapy **[9]**. The main problem of the quadruple regimen is the administration of four drugs in a complex scheme and possibly decreased compliance. Furthermore, bismuth salts are not available in all countries. However, side effects associated with the medication do not occur commonly and it can be stated that bismuth for the treatment of H. pylori is safe and well tolerated **[10]**. In Kuwait, bismuth containing quadruple therapy (Pylera) and other different regimens are available for treatment of H. pylori so we aimed to evaluate the efficacy of these different regimens in achievement of high eradication rate among Kuwaiti patients in order to establish a more effective first-line regimen for H. pylori in Kuwait.

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Subjects and Methods

Retrospective study was conducted between January 2015 and December 2016 at Gastroenterology Clinic Al-Sabah Hospital Kuwait. Patient's data collected from medical files of 510 H. pylori-infected Adult Kuwaiti (aged ≥18 years) were included in the study. All patients were diagnosed as H. pylori positive by:

1- Rapid urease test (CLO test).

2- 13 C-urea breathe test.

All patients were received 1st line therapy:

The 14-day clarithromycin based triple therapy (Esmoprazole 40mg BD plus amoxicillin 1gm BD and clarithromycin 500mg BD).

The 10-day course of bismuth containing quadruple therapy (Esmoprazole 40mg BD plus Bismuth subsalicylate 420mg, Metronidazole 375mg and tetracycline 375mg PO q6hr).

The 10-day course of Levofloxacin based triple therapy (Esmoprazole 40mg BD plus levofloxacin 500mg OD and amoxicillin BD).

The 10-day sequential therapy:

5 days of Esmoprazole 40mg BD and amoxicillin 1gm BD followed by 5 days of Esmoprazole 40mg BD plus clarithromycin 500mg BD and metronidazole 400mg BD).

All patients who included in the study completed treatment duration without drop out. Four to six weeks after completing the therapy, successful H. pylori eradication was defined by a negative 13C urea breath test. Patients who failed to cure 1 st line therapy were treated by 2 nd line therapy (bismuth containing quadruple therapy and levofloxacin based triple therapy (Esmoprazole 40mg BD plus levofloxacin 500mg once daily and 1 g of amoxicillin twice daily).

Results

Demographic data of subjects:

A total of 510 H. pylori-infected treatment-naïve subjects were included in the study (215 males, 295 female) their mean age was 45.8±16.34, their BMI was 30.02±10 and 70 patients were smokers. Four hundred and twenty nine patients treated by clarithromycin based triple therapy, 75 patients treated by bismuth containing quadruple therapy, 4 patients treated by sequential therapy and 2 patients treated by levofloxacin based triple therapy (Table 1).

Table (1): Baseline characteristics, demographic criteria of studied subjects (n=510).

Baseline characters	
Age (mean ± SD), year	45.8±16.34
Gender (female/male)	(295/215)
BMI (kg/m^2)	30.02±10.09
Smoking n (%):	
Non-smoker	408
Current smoker	70
X-smoker	32
1st line therapy n (%):	
Clarithromycin triple therapy	429
Bismuth containing quadruple therapy	75
Levofloxacin triple therapy	2
Sequential therapy	4

First-line therapy:

Overall eradication rate was 80% among all treated patients who completed the entire course of therapy and returned for follow-up Fig. (1).

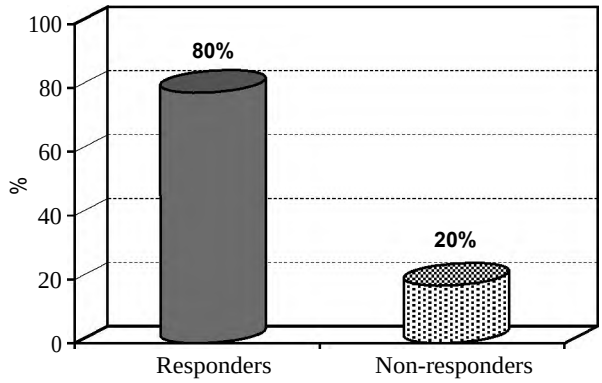

Fig. (1): Eradication rate of H. Pylori in treated patients with 1st line therapy.

Clarithromycin based therapy:

Four hundred and twenty nine patients treated by standard clarithromycin based triple therapy of them 331 patients were responders with 77% eradication rate with non-significant high cure rate among females, statistical significant low eradication rate in smokers (p<0.001), otherwise no significant difference founded regarding age and BMI between responders and non-responders to treatment (Table 2).

Bismuth based quadruple therapy:

Seventy two patients from a total of 75 patients treated by Bismuth containing quadruple therapy were responders with 96% eradication rate (Table 3).

Table (2): Patients treated by 1 st line clarithromycin based triple therapy (n=429).

Baseline data	Responders	Non-responders	*p*-value
Age (mean ± SD), year	48.32±16.71	41.63±11.78	0.27
Gender n (%):			
Male	139	39	0.698
Female	192	59	
BMI, kg/m^2	30.28±11.85	29.61±5.9	0.33
Smoking n (%):			
Non-smoker	282 (65.7%)	65 (15%)	>0.001
Current smoker	34 (8%)	24 (5.6%)	
X-smoker	15 (3.5%)	9 (2%)	

Table (3): Patients treated by 1 st line Bismuth containing quadruple therapy (n=75).

Baseline data	Responders	Non-responders	*p*-value
Age (mean ± SD), year	40.2±12.01	47.67±23.8	0.041
Gender n (%):			
Male	32	1	0.704
Female	40	2	
BMI, kg/m^2	29.52±5	28.35±2.76	0.41
Smoking n (%):			
Non-smoker	56 (74.7%)	2 (2.7%)	0.382
Current smoker	9 (12%)	0	
X-smoker	7 (9.3%)	1 (1.3%)	

Efficacy of clarithromycin based therapy versus bismuth based quadruple therapy as 1st line therapy:

Eradication rate was significantly higher in 10 days bismuth based quadruple regimen than 14 days clarithromycin basedregimen (96% vs. 77%) (p<0.001) Fig. (2).

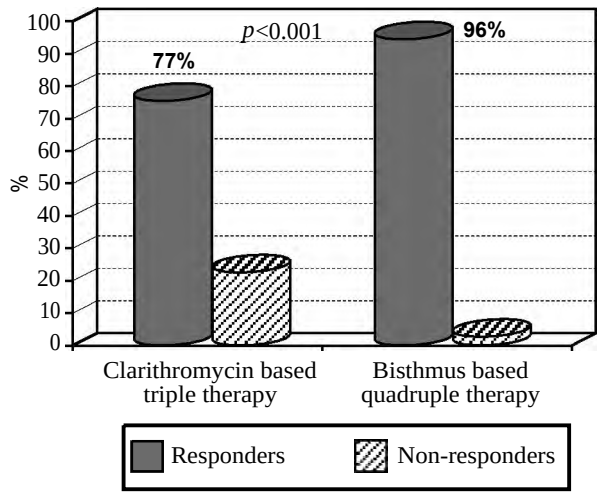

Fig. (2): Efficacy of clarithromycin based therapy versus bismuth based quadruple therapy as 1 st line therapy.

2nd line therapy (Table 4):

Bismuth containing quadruple therapy:

Seventy eight patients whose failed cure with 1 st line therapy for H. pylori eradication were treated by bismuth containing quadruple therapy showed high eradication rate with 76 cured patients, only 2 patients were non-responders and need 3 rd line therapy also there was no significant differences between responders and non-responders regarding age, gender, BMI and smoking.

Levofloxacin based triple therapy:

Fifty eight patients whose failed cure with 1 st line therapy for H. pylori eradication were treated by Levofloxacin based triple therapy (Levofloxacin 500mg OD, Amoxicilline 1g BID, Esomperazole 40mg BID) as second line therapy showed high eradication rate with 57 cured patients, only 1 patients were non-responders and need 3 rd line.

Discussion

Eradication of H. pylori infection needs combinations of 2-3 antibiotics along with a Proton Pump Inhibitor (PPI), there are different treatment regimens have been used for eradication of H. pylori infection. However, no treatment regimen can guarantees cure of H. pylori infection in 100% of patients **[11,12]**. Selection ofoptimal therapeutic regimens for treatment of patients should consistently achieve high eradication rates exceeding 90% **[13,14]**. The present study showed that the H. pylori eradication rate in standard clarithromycin based therapy was 77% which is lower than accepted eradication rate of optimal therapy for H. pylori **[13,14]** in agreement with findings of several recent large clinical trials and meta-analyses **[14-16]** and repeated samefinding of two recent clinical trials in Kuwait **[17,18]** (Alazmi et al., 2010) (Alboraie et al., 2015). These results indicate that the therapeutic effect of clarithromycin for H. pylori eradication is declining; that may be related to clarithromycin resistance of infecting H. pylori strains. Also we noticed that non-responders to clarithromycin had non-significant high BMI (29.61±5.9) consistent with previous study **[19]** that increasing suspicion of BMI role in treatment success, obese patient have high distribution volume of the drug with low concentration at gastric mucosa. Most of responders to standard triple therapy (65.7%) were non-smokers with statistically significant in comparison with non-responders (p<0.001) in agreement with study reported that Smoking is a risk factor for treatment failure may related to reduction of antibiotic delivery due to a decreased gastric blood flow, a decrease in intragastric pH in cases

of smoking, and nicotine could potentiate the vacuolating toxin activity of H. pylori in gastric cells **[20,21]**. Seventy five patients were treated by bismuth containing quadruple therapy as 1st line treatment for H. pylori had higher eradication rate (96%) in agreement with data from recent study in Kuwait **[18]** Alboraie et al., 2015 and fourth chinese national consensus report **[22]**. Also high eradication rate in consistent with previous two large studies **[23,24]**.

The present study shows that 10 days bismuth quadruple therapy wasmore effective treatment with statistically significant higher eradication rate than 14 days clarithromycin standard triple therapy (96% vs. 77%) in agreement with data from recent study in Kuwait **[18]** and consistent with previous international studies **[25-27]**. Furthermore, optimal therapeutic regimen for H. pylori as it has high eradication rates exceeding 90% consistent with previous studies **[13,14]**. A total of 136 patients failed to cured from H. pylori infection with 1 st line regimens, 98 patients (72%) of them were treated by standard clarithromycin based therapy, 3 patients (2%) were treated by Quadruple therapy while the remaining 35 patients were previously treated by other regimens (sequential, OAL). All those patients treated by 2 nd line regimens, 78 patients treated by Bismuth containing quadruple therapy (Pylera) and showed high eradication rate 97.4% in addition to 58 patients treated by Levofloxacin based triple therapy also showed high eradication rate 98.3%. Levofloxacin-containing triple therapy and bismuth-containing quadruple therapy were effective as a second-line therapy for H. pylori eradication consistent with previous study **[28]** moreover both regimens showed similar efficacy (›_90% cure rate) the same as reported by previous study **[29]**. However with increased prevalence of primary levofloxacin resistance that has been recently reported and this may affect the efficacy of levofloxacin-based regimens **[30]**. Therefore, bismuth-containing quadruple therapy continues to represent avalid second-line treatment for H. pylori eradication, particularly in areas with high fluoroquinolones resistance.

Limitation and Recommendation:

Helicobacter pylori culture and sensitivity was not routinely performed and we could not identify susceptible H. pylori strains to clarithromycin and amoxicillin-containing regimens and data regarding antibiotic resistance among H. pylori strains from Kuwait remain scarce so organized efforts are needed to document local and national patterns of resistance in order to guide the appropriate selection of H. pylori therapy.

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دراسة عن فعالية نظم العلاج المختلفة على القضاء على عدوى جرثومة المعدة الحلزونية

الجرثومة الحلزونية من العدوى الأكثر إنتشارا بين أفراد المجتمع وتنتقل العدوى للإنسان عن طريق الأطعمة الملوثة ومن الأشخاص المصابين وقد لا يعانى الشخص المصاب بالجرثومة من أى أعراض وتتسبب عند البعض فى حدوث إلتهاب مزمن بالمعدة وقرحة بالأثنى عشر وقد تتسبب فى حدوث أورام المعدة وهناك العديد من الأدوية المتوفرة للعلاج ولكن تختلف نسبة الشفاء من الجرثومة بإختلاف نوع الأدوية المستخدمة.

تهدف الدراسة إلى التعرف على فعالية الأنظمة المختلفة لعلاج الجرثومة وأجريت هذه الدراسة فى عيادة الجهاز الهضمى بمستشفى الصباح بالكويت خلال الفترة من يناير ٢٠١٥ إلى ديسمبر ٢٠١٦ حيث تم تجميع بيانات ٥١٠ من المرضى البالغين المصابين بالجرثومة ممن تلقوا العلاج والمتابعة بالعيادة الخارجية.

حيث تم علاجهم بالأنظمة المختلفة للعلاج:

١- العلاج الثلاثى المعتمد على الكلاريثروميسين.

٢- العلاج الرباعى.

٣- العلاج الثلاثى المعتمد على الليفوفلوكساسين.

وقد أظهرت نتائج الدراسة وجود تفاوت بنسبة الشفاء مع إختلاف الأدوية المستخدمة حيث تبين إنخفاض فعالية العلاج الثلاثى المعتمد على الكلاريثروميسين مما يدل على حدوث مقاومة لهذا النوع من العلاج بالكويت فى حين إرتفعت نسبة الشفاء بين المرضى الذين تلقوا العلاج الرباعى وهذا يدل على فعالية هذا النوع من العلاج فى القضاء على الجرثومة مقارنة بالعلاج الثلاثى.