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Comparison between Levofloxacin Based Therapy and Clarithromycin Based Therapy through 14 Days Period for H-Pylori Eradication

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ABSTRACT
H-pylori is a pathogen that can cause infection in human in all ages worldwide, mainly considered as a chronic infection that requires a serious treatment regimens. Most guidelines advice triple therapy including proton pump inhibitor PPI, two different antibiotics for the initial attempt to eradication of H-pylori. If the infection is persistent after the first therapy trial, a quadruple therapy which include PPI, Bismuth sub-citrate and two different antibiotics is recommended for second attempt.
This study was conducted in alsamawa city/ Iraq to compare the efficacy of levofloxacin versus clarithromycin in the eradication of H.pylori .it was carried out from october 2018 to march 2019. A total of 103 patients treated with one of these regimens were interviewed after treatment completion (group A –50 patients, group B –53 patients). Collected data included age, gender, chronic diseases, smoking and indication for treatment, side effects and adherence.
The eradication rate obtained with clarithromycin was significantly lower than with Levofloxacin-based therapy. From our experimental work, the side effect with clarithromycin more than with levofloxacin.
In Iraq as in other developing countries, almost all antibiotics are easy to get from local pharmacies even without doctor's prescription so there is a significant misuse of antibiotics, so the antibiotic resistance is higher.
Keywords: Levofloxacin, Clarithromycin, antibiotic resistance, Helicobacter Pylori.
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INTRODUCTION
H-pylori is a pathogen that can cause infection in human in all ages worldwide, mainly considered as a chronic infection that requires a serious treatment regimens, the data base showed that around 50% of the individuals affected by this bacteria are of young ages in developing countries due to poor personal hygiene. [1,2]
The frequency of infection due to H. pylori is nearly 50% in the world and in developing country is as high as 80%-90%. [3]
This bacteria is a gram negative, urease positive, this can allow it to survive in low pH medium of the stomach. The bacteria is highly motile which helps it to attack the gastric mucosa before been destructed by the high acidity. [4]
The first virulence factor used for the diagnostic process for the H.Pylori was urease enzyme test. [5]
Ammonia liberated by the action of urease on the maximal concentration of urea in the gastric fluid is the causative agent of induced cell injury of the stomach epithelium. [6]
The most observable symptoms due to Hpylori infection are chronic gastritis, peptic ulcer, dyspepsia, gastric cancer. A serious intervention should take place immediately once the H-pylori infection is diagnosed and confirmed because most of the patients around the world remain asymptomatic for a long period of time so this may lead to complications of the pateint's symptoms and high risk of permanent damage such as gastric ulcers or cancer.[7,8,9]
Gastric cancer may possibly prevented by the eradication of H-pylori as many experts and scientist believe. [10,11]
Moreover, there is documented data suggesting a relationship between the H.pylori infection and gall stones formation based on studies in Iran. [12]
Most guidelines advice triple therapy including proton pump inhibitor PPI, two different antibiotics for the initial attempt to eradication of H-pylori. If the infection is persistent after the first therapy trial, a quadruple therapy which include PPI, Bismuth sub-citrate and two different antibiotics is recommended for second attempt. A recent study and survey confirmed that 7-days standard triple therapy for H-pylori treatment is the popular regimen in the Asia-pacific area. [13]
But this standard triple therapy use has declined in rate for less than 80% in most countries worldwide due to high rates of antibiotic resistance. [14,15,16,17]
The identification of the cause for the triple therapy failure result in the Clarithromycin resistance which is largely responsible for this problem. [18,19]
A global studies were done to investigate the high rates of Clarithromycin resistance that included 11697 cases in 2009, and the cases were reported resistant 11.1% in Europe, Asia 18.9% and America 29.3%. [20]

MATERIALS AND METHODS
This study was conducted in alsamawa city/ Iraq to compare the efficacy of levofloxacin versus clarithromycin in the eradication of H.pylori .it was carried out from october 2018 to march 2019. Exclusion criteria of the study were age below 18 and more than 60, history of renal and liver diseases, allergic reaction to the treatment, pregnancy, and use of antibiotics for 4 weeks before the study.
Our primary end point was H.pylori infection eradication and secondary endpoint wasthe drug side effects, Adult patients infected with H. pylori confirmed their infection by Serology or stool antigen and treated with either standard

treatment (group A) or Levofloxacin treatment (group B) were considered for inclusion.

The treatment regimen was chosen according to their physicians' preference. Other inclusion criteria were: (1) age over 20 years-old, (2) absence of known allergies for antibiotics used in either regimen, (3) signed informed consent.

A total of 103 patients treated with one of these regimens were interviewed after treatment completion (group A –50 patients, group B –53 patients). Collected data included age, gender, chronic diseases, smoking and indication for treatment, side effects and adherence.

Patients in group A were treated with standard therapy for two weeks: PPI twice daily + Amoxicillin 1 g twice daily for 5 days; followed by PPI twice daily + Clarithromycin 500 mg twice daily.

Group B patients were treated with Levofloxacin therapy for two weeks: PPI twice daily + Amoxicillin 1 g twice daily for 5 days followed by PPI twice daily + Levofloxacin 750 mg once daily.

Table 1: Demographic data of the two group

Demographic data	Group A	Group B
Sex	Male (24) Female (26)	Male (29) Female (24)
Age	20-30 (9) 31-40 (14) 41-50 (13) 51-60 (14)	20-30 (11) 31-40 (16) 41-50 (15) 51-60 (11)
DM	9	6
HT	10	8
hyperlipidemia	6	7
Smoker	14	12

Demographic characteristics of studied population by the studied two groups

Table 2: Distribution of the two studied groups (A and B) according to Gender.

Gender	Treatment		P value
	Group A	Group B	
Male	24 (48%)	29 (54.7%)	0.557
Female	26 (52%)	24 (45.3%)	
Total	50 (100%)	53 (100%)	
P value	0.777	0.492	

* represents a significant difference at $p<0.05$.

Table 3: Distribution of the two studied groups (A and B) according to Age.

Age	Treatment		P value
	Group A	Group B	
20-30	9 (18%)	11 (20.8%)	0.862
31-40	14 (28%)	16 (30.2%)	
41-50	13 (26%)	15 (28.3%)	
51-60	14 (28%)	11 (20.8%)	
Total	50 (100%)	53 (100%)	
P value	0.715	0.667	

* represents a significant difference at $p<0.05$.

RESULTS

103 patients were enrolled in two groups (group A contain 50 and group B contain 53). In group A, four patient were lost and three patient were lost in group B. Three patients were lost to follow-up and three patients discontinued therapy because of adverse events. all of which, they have been excluded from our data and results. There were no differences between groups in terms of gender, age, smoking habits and indications for treatment. The eradication rate obtained with clarithromycin was significantly lower than with Levofloxacin-based therapy. From our experimental work, the side effect with clarithromycin more than with levofloxacin. patient who had suffered from side effect in group A were reported as the following: Nausea(29), vomiting (5), skin rash (13), dizziness (18), bloating (19), dry mouth (4), dark stool (9), metallic taste (32) while with group B Nausea (22) ,vomiting (2) , skin rash (9), dizziness (17), bloating (14) , dry mouth (2), dark stool (7). There

were no patients complained from the occurrence of metallic taste as a side effect in group B.

Table 4: Eradication success with the two types of treatment

Groups	n	%
Group A	37/50	74%
Group B	44/53	83%

Table 5: Side effect of treatment

Side effects	Group A	Group B
1-nausea	29	22
2-diarrhea	23	21
3-headache	23	19
4-metallic taste	32	_
5-epigastric pain	31	34
6-dark stool	9	7
7-dry mouth	4	2
8-bloating	19	14
9-dizziness	18	17
10-skin rash	13	9
11-vomiting	5	2

Table 6: Distribution of the two studied groups (A and B) according to clinical Side effects.

Side effects	Treatment		P value
	Group A N=50	Group B N=53	
Nausea	29 (58%)	22 (41.5%)	0.094
Diarrhea	23 (46%)	21 (39.6%)	0.513
Headache	23 (46%)	19 (35.8%)	0.295
Metallic taste	32 (64%)	0 (0%)	<0.0001*
Epigastric pain	31 (62%)	34 (64.2%)	0.821
Dark stool	9 (18%)	7 (13.2%)	0.502
Dry mouth	4 (8%)	2 (3.8%)	0.360
Bloating	19 (38%)	14 (26.4%)	0.208
Dizziness	18 (36%)	17 (32.1%)	0.674
Skin rash	13 (26%)	9 (17%)	0.264
Vomiting	5 (10%)	2 (3.8%)	0.210

* represents a significant difference at p<0.05.

Clinical characteristics of studied population by the studied two groups

Table 7: Distribution of the two studied groups (A and B) according to clinical characteristics.

Characteristics	Treatment		P value
	Group A N=50	Group B N=53	
DM	9 (18%)	6 (11.3%)	0.337
HT	10 (20%)	8 (15.1%)	0.512
Hyperlipidemia	6 (12%)	7 (13.2%)	0.854
Smoker	14 (28%)	12 (22.6%)	0.532

* represents a significant difference at p<0.05.

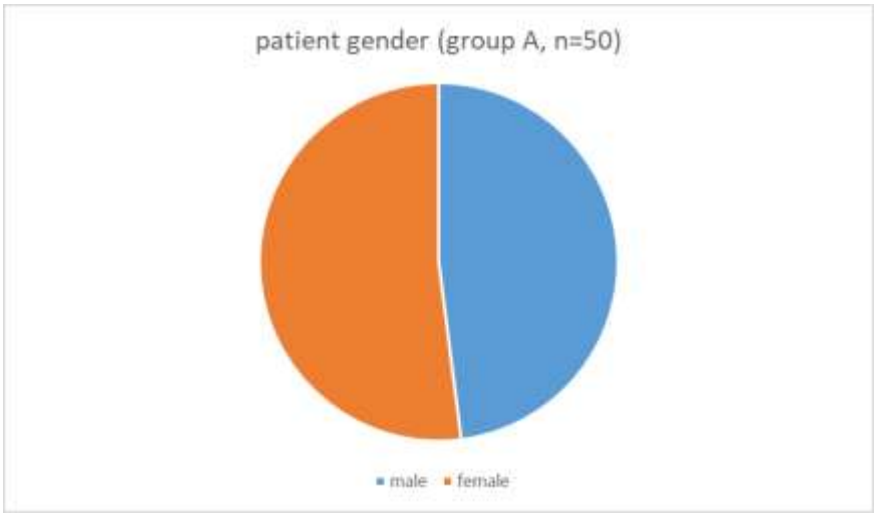

Figure 1: Patients gender distribution, group A.

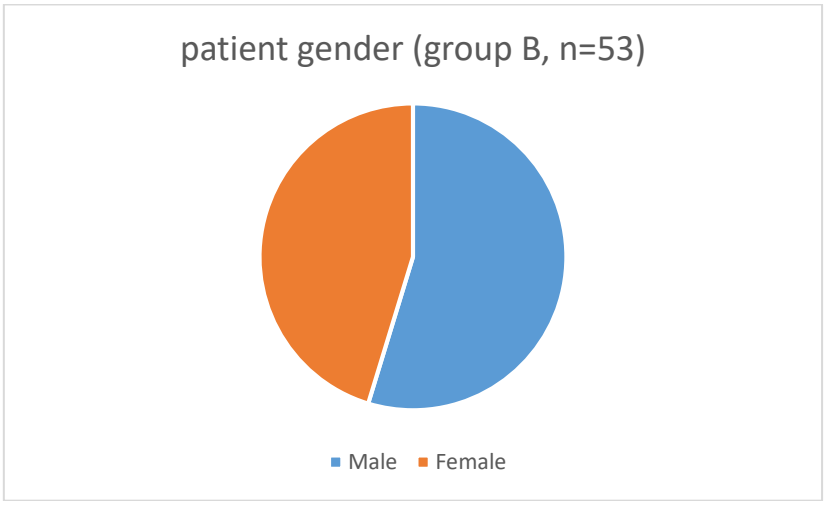

Figure 2: Patients gender distribution, group B.

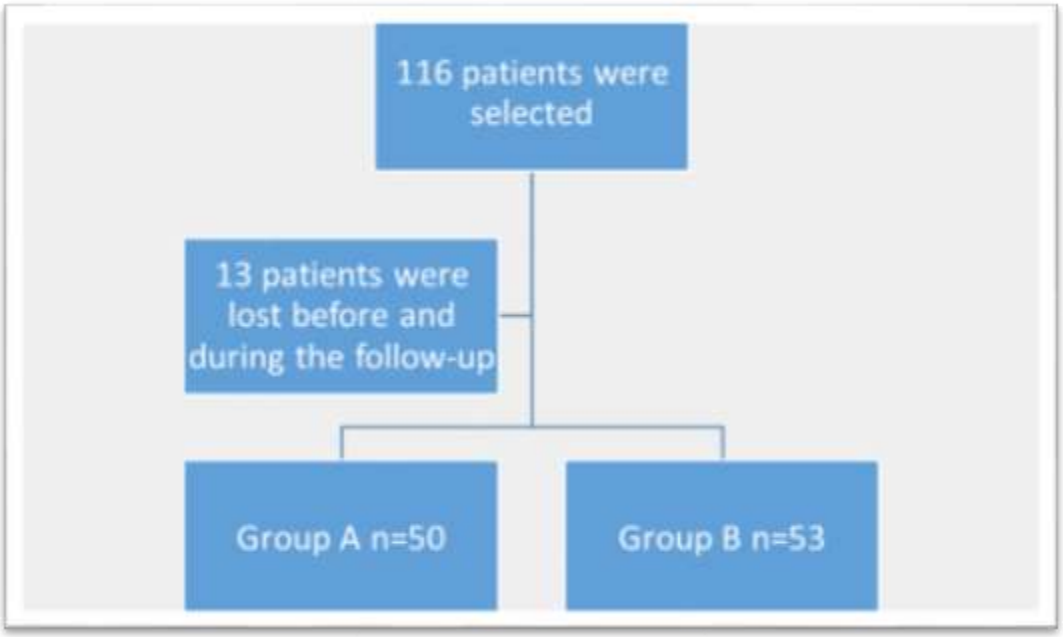

Figure 3: The total number of participants illustration.

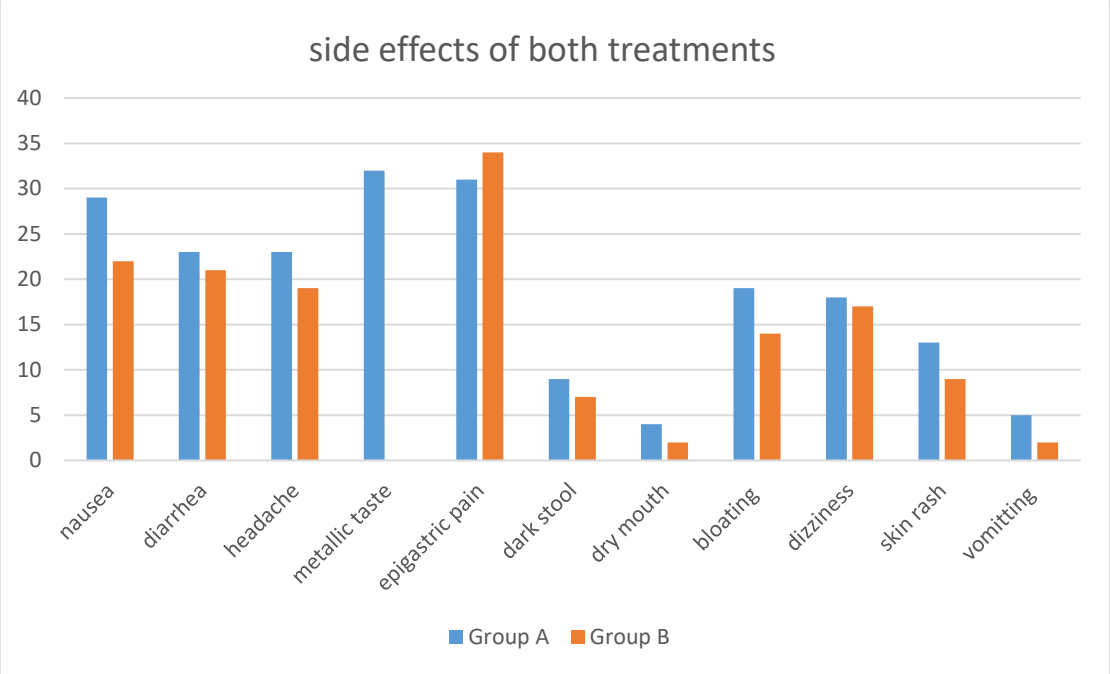

Figure 4: Side effect for group A and group B.

DISCUSSION

We assumed that the failure of the treatment was due to antibiotic resistance cause in our area it is crucial to culture endoscopic biopsy samples from the patients, due to difficulty of H.pylori organism culturing process and this technique was not available. So we cannot confirm that the cause of our results is the drug resistance. Upon the information and data provided from the patients history the adherence rate was granted. also we cannot confirm that all the patient participated in our study were naïve to the classes of antibiotics involved in our research because there are no recorded medical data to each patient in Iraqi hospitals and private clinics.

. in Iraq as in other developing countries, almost all antibiotics are easy to get from local pharmacies even without doctor's prescription so there is a significant misuse of antibiotics.

Medications used in this study were all provided by private sector pharmacies in alsamawa city form different brands manufacturers.

There were no patients complained from the occurrence of metallic taste as a side effect in group B.

Our study showed that the failure of treatment regimen containing clarithromycin is higher which is supported by international data recoded which state that the resistance of clarithromycin in treating H.pylori ranging from 5.46% to 30.8%. [21]

Finally, it is important to mention that the questions asked to the patients related to this study was written in English language, but we explained the questions in Arabic language to patients due to their poor education, and then we recorded the answers and data.

CONCLUSION

Levofloxacin-based regimen is more effective than clarithromycin therapy regimen, with less side effects reported by the patients participated which is critical parameter to avoid the discontinuation of therapy by the patient due to side effects complication. It is recommended that levofloxacin regimen be used as the first-line therapy, especially in areas with high levels of resistance to clarithromycin. More studies with larger numbers of samples are needed to further evaluate the efficacy of this regimen in different parts of the country.

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