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ORIGINAL ARTICLE

A Comparison Between 10-Day and 12-Day Concomitant Regimens for Helicobacter Pylori Eradication

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ABSTRACT

H. pylori (Helicobacter pylori) is the most prevalent infection worldwide which leads to gastric ulcer and cancer. In our research work, patients infected with H. pylori were given concomitant treatment for 10 and 12 days and compared to find the efficiency of treatment.

Objective: The objective of this study is to find a cost-effective therapeutic method for the treatment of H. pylori. Previous 14-day treatment was effective but it was expensive due to the high cost of antibiotics as well as the negative side effects of the treatment, so an alternative method is required to reduce the need of costly antibiotics and the duration of treatment.

Study design: It is a comparative study with statistical approach, conducted in the medicine department of Sialkot Medical College, Sialkot for the duration of six months from June 2021 to November 2021.

Methods: For this study, 196 patients with gastric ulcers were selected and confirmed H. pylori positive by a diagnostic test. These patients randomly distributed into two groups and given treatment for 10 and 12 days respectively. UBT was used to find either H. pylori is eradicated or not. “Registry of clinical trials” registered this experiment.

Results: For this research work, 196 patients were selected, after the concomitant therapy eradication rate was analyzed that comes out as 83 % (CI 95.0%: 76-90) and 88 % (CI 95%: 82-94) for 10 and 12 day therapy, respectively (p = 0.23). Then, prediction of per-protocol eradication was done and it came out as 85% (CI 95%: 79-92) and 92% (CI 95%: 87-97), respectively (p = 0.18). When side effects were compared between two groups, no statistical difference exist between two (3.5% vs. 8.0%; p = 0.419).

Conclusion: All the results suggested that the concomitant therapy that was given for 12 days was more effective for treatment and per-protocol assessment. For the reduction of the cost of antibiotics, 12 day treatment is more effective for treatment as well as the replacement of 14 day treatment that was suggested by international rules.

Keywords: Helicobacter pylori, gastric ulcer, concomitant therapy, treatment efficacy, H. pylori eradication.

INTRODUCTION

Helicobacter pylori infected more than half of the population globally. This infection leads to different diseases like peptic ulcers and different malignancies of the gastric zone i.e. lymphoma and adenocarcinoma. H. pylori can reside within the host lifelong if it remains untreated. About 85% of the people infected with H. pylori develop a mild asymptomatic gastric infection but 15% of the patients may develop serious gastric issues like peptic ulcers and gastric cancer[1-2]. There are three different virulence factors involved in the pathogenicity of H. pylori, the first one is colonization, the second one is an immune escape and the last one is induction of disease. All these virulence factors play their role in the colonization of bacteria accompanied by chemotaxis, adhesion, and flagella. When any of these factors is knocked out, Helicobacter pylori loses its ability to colonize. These virulence factors facilitate alternative treatments and therapies for the elimination of H. pylori[3-4].

Multiple studies of the present decade put efforts to introduce more valuable rehabilitation methods to treat H. pylori. In the past years, to treat infection of H. pylori, clarithromycin therapy was used, but this therapy's efficiency was below 80 % due to bacterial resistance.[5]

The report of the Maastricht consensus suggests that concomitant treatment of 14- days is considered enough for the first-line treatment of H. pylori, in case of bacterial resistance to metronidazole and clarithromycin is lower than 15 %. This concomitant therapy includes a drug specified for proton pump inhibition along with clarithromycin, metronidazole[6-7], and amoxicillin. The majority of countries considered this concomitant therapy, an effective method for the complete treatment of H. pylori’s infection[8].

According to reports of the Maastricht V consensus, a treatment of 14 days is effective, in case of severe infection, but to treat the cases with low prevalence, a duration of 10 to 12 days will also be effective. So, in this study, the effects of antibiotics of this concomitant therapy of H. pylori treatment were compared by day alteration (10 and 12 days) [9-10].

MATERIALS AND METHODS

It is a comparative study with statistical approach, conducted in the medicine department of Sialkot Medical College, for the duration of six months from June 2021 to November 2021. For this research study, 196 patients with gastric ulcer were selected. These patients were diagnosed with H. pylori infection by urease test and further confirmation was done by histological assessment of biopsy samples (gastric). All of these patients were not given any treatment to eradicate Helicobacter pylori. Patients were randomly distributed into two groups i.e. 98 patients in each group. One group was given concomitant treatment for 10 days and the other group was given treatment for 12 days. The concomitant regime therapy includes metronidazole (500 mg), clarithromycin (500 mg), amoxicillin (1000 mg), and pantoprazole (40 mg).

For the random distribution of patients, the block randomization method was employed, according to this method classification of patients was carried out on the basis of sex and age. The patients were arranged in five groups. During the selection of patients, all those patients were excluded that were pregnant or breastfeeding their young ones and had a history of gastrointestinal surgery or malignancy, and using anti-convulsant or anticoagulant dosage.

All the experimental patients were given instructions and precautions related to treatment, and all the patients were advised for a quick visit to the doctor in case of any emergency. For estimation of effective treatment or any negative effect, a follow-up visit was arranged for patients in these two weeks of treatment. Overall, the effect of treatment along with adverse effects was carefully noted and analyzed. Concurrence with treatment was predicted on the basis of the interview and it was considered excellent if patients took 90 %, if the patient took 70 to 90 %, it is considered as good if a patient took less than 70 %, the situation is considered poor. The level of adverse effects was also assigned different ranks such as mild, moderate, and severe. The effects of therapy were considered severe if they restrict activities of life, in the case of moderate effects activities, are restricted partially, and in mild situations, no obstruction of activities is observed.

After the complete treatment of 8 weeks, UBT (^{14}C Urea breath test) was used for the prediction of the presence of Helicobacter pylori. To proceed with this experiment, the written consent of the patients was taken. The approval of this research work was by the "Ethics Committee of University and "Registry of Clinical Trials" approved and registered this experiment for the treatment of helicobacter pylori. SPSS software tool was used for data analysis. For appropriate Chi-test, logistic regression and t-test were used. Intention to treat analysis was applied to all experimental patients. The pre-protocol analysis includes only those patients with 90 % amenability. When the p-value is less than 0.05, it is considered significant.

RESULTS

196 patients were included in this study. 98 of these patients were given 10 days' concomitant treatment and the remaining 98 patients were given 12 days' concomitant therapy. The consent was taken from all the patients. And the mean ages of the participating patients came out to be 46 and 44 years respectively. The demographic profile and the endoscopic results of the patients of both groups are shown in the table.

Table 1: Demographic features and endoscopic results of the patients in both groups

Patient's profile	10-days concomitant treatment N (%)	12 days concomitant therapy N (%)	P value
Male/female	44/55	44/55	0.99
Mean age ± SD (years)	46 (±14) years	44 (±13) years	0.35
Current smoking habits (%)	11 (11.2%)	7 (7.1%)	0.99
Gastrointestinal bleeding history (%)	6 (6.1%)	5 (5.5%)	0.99
Usage of non-steroidal anti-inflammatory medicine	9 (9.1%)	11 (11.2%)	0.65
Endoscopic results			
			0.24
Duodenal ulcer	43 (43.8%)	54 (56.2%)	
Gastric ulcer	14 (14.5%)	13 (13.2%)	
Duodenal and gastric ulcer	1 (1%)	2 (2.0%)	
1st degree gastric cancer	4 (4%)	1(1%)	
Gastric adenomatous polyp	1 (1%)	1(1%)	

Out of all the participating individuals (196), the 194 patients completed whole study. As per intention-to-treat findings the rates of eradication are 83.6% with 95% confidence interval (CI): 76-90 and the eradication rate in case of 10 days' concomitant group came out to be 88% with 95% confidence interval CI: 82-94. In case of 12 days' concomitant group, the rates were same as in 10 days' group. 1 patient in the 10 days' group and 1 patient in the 12 days' group halted the study because of severe side effects of the treatment. (p=0.1). The compliance in both groups (10 days' group and 12 days' group) came out to be excellent 97% in case of patients included in 10 days' group and 87% in case of other group (p=0.03). Just like that the eradication rates per protocol were 85% (CI: 79-92) and 92% (CI: 87-97) in case of both groups respectively. The logistic regression analysis showed that no demographic or any endoscopic aspect was linked with the success of the treatment.

The rate at which this treatment showed severe side effects came out to be 32% and 38% in case of 10 and 12 days group respectively. The findings showed that the signs and symptoms were mild and only 3% and 8% of the patients in both groups respectively showed adverse symptoms. The rates were not any different statistically in case of both groups. According to patients the most common symptom reported was bitter taste.

Table 2: Rate and adverse side effects of treatment in both groups

Side effects	10 days treatment group N (%)	12 days treatment group N (%)	P value
Diarrhea	1 (1%)	5 (5.1%)	0.2
Bitter taste	13 (13.2%)	16 (16.3)	
Anorexia	1 (1%)	0	
Dizziness	1 (1%)	1 (1%)	
Nausea and vomit	1 (1%)	5 (5.1%)	
Rash	1 (1%)	0	
Epigastric pain	4 (4.1%)	2 (2.04%)	
Bloating	1 (1%)	0	
Headache	1(1%)	1 (1%)	
Malaise	4 (4.1%)	2 (2.04%)	
Abdominal cramp	1 (1%)	1 (1%)	
Dry mouth	0	1 (1%)	
Palpitation	0	1 (1%)	
Severity of the side effects			0.4
Mild	12 (12.6%)	15 (15.3%)	
Moderate	16 (16%)	14 (14.2%)	
Severe	3 (3.0%)	8 (8.1%)	

DISCUSSION

After studies it was found that a total of 85% of the individuals from the 10 days' treatment group and 92% of the patients from the 12 days' treatment group had ability to eradicate H. pylori according to the protocol of the analysis[11]. The ideal treatment to kill H. pylori would be the regime that can eradicate this organism in more than 90% of the cases. But according to the reports from Toronto consensus the treatment that can eradicate more than 85% of H.pylori can also be accepted. Therefore, as per our results we can confer that 12 days' treatment gives ideal result but 10 days' treatment is also accepted.[12-13] According to studies by other countries the eradication rate was acceptable in 14 days' treatment, or in some cases a shorter a shorter duration of treatment could also be accepted. In 2013, a study was carried out where Zullo and his colleagues showed that the H. pylori eradication was made possible by a 5 days' treatment plan in Italy. Again in 2013 Molina-infante stated that their results showed 91% eradication by using a 14 days' treatment in Spain[14-15].

According to studies carried out in 2014, they found that the rate of eradication was enhanced to 86% after a 14 days' treatment carried out in Italy. And similar results were obtained in Spain as well. Studies were also carried out in Asian countries as well and there the eradication rate was 94% after 10 days of treatment in South Korea.[16-17] In 2017, Parks and his colleagues reported that 95% and 98% eradication was possible after a 10 days and 14 days' treatment in Korea respectively. In the same year another finding showed that eradication was possible by 95% after a 10-days treatment. Studies were also carried out in Taiwan, which is country rich in H. pylori cases, that an accepted treatment was found after 7, days, 10 days and 14 days[18]. As per Maastricht V Consensus findings the concomitant treatment is the most effective and accepted treatment and this treatment is accepted when the resistance to the metronidazole and clarithromycin is less than 15%. The studies showed that the duration of treatment is 14 days, if any treatment is of less than 14 days then its efficiency will also be low[19].

According to the results of our study, it was found that the 10 days and 12 days' treatment both could be used as a first line treatment to eradicate H. pylori but the results can only be attributed in regions where the resistance pattern is same. If some region has high H. pylori resistance, then there this treatment will have different consequences. According to recent studies the resistance to clarithromycin is more than 15% in our region, but the dual resistance rate is not defined yet. Therefore, the study is applicable in those regions having 15% or less resistance to clarithromycin[20]. One more point to note here is that one of the issues that scientists face when looking for H. pylori treatment is the adverse side effects of the treatment. In our study it was found

that although the adverse side effects were not so statistically different in both groups of the study, but still the group 1 that was receiving 10 days' treatment showed less adverse signs and symptoms as compared to other group. The ideal treatment should have less than 5% adverse signs and symptoms. Here in our study in case of 10 days' treatment the patients were showing less than 5% of the adverse effects[21].

Limitations: The limitations of the study were that the strain of H. pylori was not available. Also it could prove to be effective if the arm of 14- days' concomitant therapy was also used. However, the study is discussing 10 days and 12 days' eradication of H. pylori and it is concluded that the 10 days and 12 days' treatment looks very effective for first line treatment for H. pylori even in the areas that have elevated resistance level[22].

CONCLUSION

Although both groups showed no difference in side effects, but still 10 days' treatment group showed less side effects as compared to 12 days' treatment. However, the eradication rate of 12 days' treatment is more than 10 days' treatment in case of our studies. The 12 day treatment has more treatment efficacy, as well as it also help to reduce the cost of antibiotics. It is the best replacement of 14 day treatment that was suggested by international rules.

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