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• BRIEF REPORTS •

Maastricht II treatment scheme and efficacy of different proton pump inhibitors in eradicating *Helicobacter pylori*

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Abstract

AIM: The Maastricht II criteria suggest the use of amoxicillin and clarithromycin in addition to a proton pump inhibitor over 7-10 d as a first line therapy in the eradication of *Helicobacter pylori (H pylori)*. For each proton pump inhibitor, various rates of eradication have been reported. The present study was to compare the efficacy of different proton pump inhibitors like omeprazole, lansoprazole and pantoprazole in combination with amoxicillin and clarithromycin in the first line eradication of *H pylori* and to investigate the success of *H pylori* eradication in our district.

METHODS: A total of 139 patients were included having a *Helicobacter pylori* (+) gastroduodenal disorders diagnosed by means of histology and urease test. Besides amoxicillin (1 000 mg twice a day) and clarithromycin (500 mg twice a day), they were randomized to take omeprazole (20 mg twice a day), or lansoprazole (30 mg twice a day), or pantoprozole (40 mg twice a day) for 14 d. Four weeks after the therapy, the eradication was assessed by means of histology and urease test. It was evaluated as eradicated if the *H pylori* was found negative in both. The complaints (pain in epigastrium, nocturnal pain, pyrosis and bloating) were graded in accordance with the Licert scale. The compliance of the patients was recorded.

RESULTS: The eradication was found to be 40.8% in the omeprazole group, 43.5% in the lansoprazole group and 47.4% in the pantoprazole group. Sixty-three out of 139 patients (45%) had eradication. No statistically significant difference was observed between the groups. Significant improvements were seen in terms of the impact on the symptom scores in each group.

CONCLUSION: There was no difference between omeprazole, lansoprazole and pantoprazole in *H pylori* eradication, and the rate of eradication was as low as 45%. Symptoms were improved independent of the eradication in each treatment group. The low eradication rates suggest that the antibiotic resistance or the genetic differences of the microorganism might be in effect. Further studies are required to verify these suggestions.

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INTRODUCTION

So far, no ideal treatment exists although there have been plenty of treatment schemes in the eradication of *Helicobacter pylori* (*Hp*). Therefore, research on this subject has substantially increased. In order to achieve the optimal treatment regimen various combinations including antibiotics and antisecretory agents have been tested[1]. In 2000, use of amoxicillin and clarithromycin for a period of at least 1 wk in combination with a proton pump inhibitor (PPI) was suggested[2]. Diverse eradication rates have been reported with this specific treatment scheme[3-6]. Up to date, five diverse PPIs have been launched in our country. The outcomes obtained from studies related with those inhibitors have resulted in confusing eradication rates.

The present study aimed to investigate the efficacy of three different PPIs given in combination with antibiotics, which have been accepted to be standard in the eradication of Hp and the success of *Hp* eradication by this standard treatment.

MATERIALS AND METHODS

Between September 2001 and July 2002, 139 patients with gastritis, gastric ulcer and duodenal ulcer were enrolled in this study. All patients were positive in urease test and histopathological examination for *Hp*. Patients with a concomitant serious illness and a history of gastric surgery, pregnancy, patients taking antibiotics, H-2 receptor blockers or on PPI treatment within the last two months, being allergic to macrolides and having a previous eradication treatment were excluded. Their written informed consent was received. They were randomized to take omeprazole 2×20 mg/d (OAC), lansoprazole 2×30 mg/d (LAC) or pantoprazole 2×40 mg/d (PAC) plus amoxicillin 2×1 000 mg/d and clarithromycin 2×500 mg/d for 14 d. All of the eligible patients had standard laboratory tests, and their history, physical examination and concomitant treatment regimens were recorded. Their complaints (epigastric pain, bloating, nocturnal pain and pyrosis) were graded in accordance to the Licert scale (0=none, 1=mild, 2=moderate, 3=severe, 4=very severe). Two biopsies were taken from the antrum and corpus for pathology, and a biopsy from the antrum for urease test. The pathological assessment was based on the Sidney classification for gastritis. 4 wk after the therapy the side effects and alterations were re-evaluated, and a blinded gastroenterologist repeated the endoscopical examination. Negative *Hp* in both urease test and biopsy was accepted as eradication.

To understand the compliance, the patients were asked to report how many prescribed drugs they used (100%-forgotten for 0 d, 80-99%-forgotten only for 1 d, 60-79%-forgotten for 2 d and below 59%-forgotten more than 2 d). The side effects were recorded.

Statistical analysis

The definitive statistics were calculated (mean±SD, numbers and % values). For age comparison in three groups, simple analysis of variance was used while gender, smoking, NSAID use, alcohol consumption, eradication status and relationship between the three groups were determined by Pearson chi-square test, which was also used to determine the relation between the eradication status and antral gastritis and pangastritis plus smoking and histological activity in the antrum prior to eradication. The differences in the symptom score between the eradicated and non-eradicated were investigated by Wilcoxon test before and after the eradication. Furthermore, t-test was applied to compare the improvement rates in the separate symptom score between the eradicated and non-eradicated in relation to the difference between the rates in 3 groups.

RESULTS

Table 1 gives the demographical characteristics of the patients in the three groups. Of the patients, 73(58.3%) were women, and 66(41.7%) were men, and the average age was 47.9±11.8 years. The patient compliance was 95%. Two patients from each group discontinued the therapy for 8 d due to side effects (nausea, vomiting, and diarrhea). The endoscopical lesions are shown in Table 2. The eradication was found in 22 out of 49 patients (40.8%) in the omeprazole group, 20 out of 46 patients (43.5%) in the lansoprazole group, and 21 out of 44 patients (47.4%) in the pantoprazole group. There was no any differences between three groups (P>0.05). The overall eradication rate was 45%. Twenty-two out 62 patients (37%) with antral gastritis had eradication while 19 out of 34 patients (55%) with pangastritis had eradication (P<0.05). No correlation was found between eradication and smoking and histological activity in the antrum prior to eradication (P>0.05). Significant improvements were observed in the symptom score between the eradicated and non-eradicated compared to pre-eradication status (P<0.05), but no significant differences were found between the groups.

Table 1 Demographic features of study population

	OAC	LAC	PAC	*P*
Patient number	49	46	44	NS
Female / Male	26 / 23	23 / 23	24 / 20	NS
Year				
Mean	47.5±13.4	45.7±12.5	44.5±13.5	NS
Range	20-75	21-73	20-70	NS
Smoking	7 (14.2%)	6 (13%)	6 (13.6%)	NS
NSAID	9 (18.3%)	8 (17.3%)	8 (17.1%)	NS
Alcohol	(22.4%)	9 (19.5%)	10 (22.7%)	NS

Table 2 Endoscopic findings

Finding	Patient *n*, (%)
Antral gastritis	62 (44.5)
Pangastritis	34 (24.5)
Bulbitis	14 (10)
Bile reflux gastritis	12 (8.6)
Duodenal ulcer	7 (5.3)
Atrophic gastritis	6 (4.3)
Gastric ulcer	4 (2.8)

DISCUSSION

Recently, triple therapies including a PPI and two antibiotics have been found to be the most effective eradication regimens in the treatment of *Hp* eradication[7,8]. The most common antibiotics used in the triple therapies were amoxicillin, clarithromycin and metronidazole[7,8]. Treatment regimens including PPIs are now used at all stages of the *Hp* eradication. The highest eradication rates for *Hp* (80-95%) have been achieved by using antibiotics at least for one week[9]. However, even the highest doses of omeprazole or an increased treatment duration for 2 wk did not provide 100% eradication[10-13]. In the European consensus meeting, it suggested that PPI treatment for one week including amoxicillin and clarithromycin was the first line therapy[10].

Our study showed that triple therapy for 2 wk was safe and well tolerated. The patient compliance was 95%. However, the eradication rate was 45%. Similarly in a study from Adana (Southern Anatolia), a two-week usage of lansoprazole, amoxicillin and clarithromycin resulted in 59% eradication[14]. In Istanbul (North Western Anatolia) and Nigde (Central Anatolia) the eradication rates were found below 50% in two different studies[15,16].

Similarly, in Iran, the eradication rates with omeprazole, amoxicillin and clarithromycin were found to be below 70%[17]. Also, some European studies reported similar rates of eradication[12,13,18-20,22,23]. Rinaldi[21] studied 278 patients by using a treatment regimen similar to ours (omeprazole, lansoprazole and pantoprazole in combination with amoxicillin and clarithromycin for one week). The eradication rates were found to be 86%, 74% and 76% respectively, which were higher than our results, yet far beyond the acceptance levels[21].

Different eradication results obtained by similar treatment regimens suggest that resistance to antibiotics, virulent factors of *Hp* or type of gastroduodenal disorders of patients might have played a role in the outcomes. In some of the studies resulted in lower eradication rates, the resistance to clarithromycin was as high as 10%[24]. In a study carried out in Ankara (Central Anatolia), the resistance to clarithromycin was 11.4%[25]. An Italian study found the primary resistance to clarithromycin was 3.2%[26]. The primary resistance to macrolides was between 3-12% in Europe and 2-10% in the United States[27,28]. We did not investigate the resistance to antibiotics in the present study. However, we believe that the resistance to antibiotics might have played an important role in our results. Also the majority of the events were from the non-ulcer dyspepsia group, therefore this might have an effect on the result because a lower rate of eradication was reported in patients with non-ulcer dyspepsia compared to those with peptic ulcer[24,29]. Our results showed that patients with pangastritis had a better eradication than those with antral gastritis (P<0.05). This was in compliance with the correlation between the severity of gastritis and the rate of eradication[30,31].

In conclusion, our findings from Mersin (Southern Anatolia) with lower eradication rates obtained by similar treatment regimens compared to other districts in Turkey and in the World demonstrate that it is necessary to find out a treatment scheme specific to the district. The findings prove that standard treatment regimens might not be suitable and therefore establishment of a new treatment protocol in accordance with the results obtained locally is inevitable. We believe that the lower rates of eradication might have resulted from the resistance to antibiotics.

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