The efficiency of Levofloxacin Containing Sequential Therapy with or without Bismuth, in Helicobacter Pylori Eradication, in Non-ulcer Dyspepsia

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Abstract

Introduction **: The aim of this study is to determine the efficiency of levofloxacin containing sequential therapy with or without bismuth in Helicobacter pylori (Hp) eradication in nonulcer dyspepsia.**

Materials and Methods: One hundred and ninety Hp-positive patients with the pre-diagnosis of nonulcer dyspepsia were included in this study. Patients were randomized into 2 groups and 95 individuals were included in each group. The first group was administered levofloxacin containing sequential therapy with bismuth, whereas the second group was administered only levofloxacin containing sequential therapy. Rates of therapy discontinuation and eradication success were compared between the 2 groups. Furthermore, symptomatic healing rates were compared between patients in whom Hp eradication was achieved and in whom it was not achieved.

Results **: Ninety-one patients from each group applied for follow-up after treatment. It was found that 7/91(7.6%) patients from the first group and 5/91(5.4%) patients from the second group did not complete the therapy (p >0.05). In patients who completed therapy, Hp eradication was achieved in 72 out of the 84 patients (85.2%) from the first group and 71 out of 86 patients (82.6%) from the second group (p > 0.05). In addition, symptomatic healing occurred in 125 out of 143 patients (87.4%) in whom Hp was eradicated and 12 out of 27 (44.4%) patients in whom Hp was not eradicated (p < 0.001).**

Discussion **: Levofloxacin containing sequential therapy for 14 days is quite effective and well-tolerated choice for Hp eradication. However, adding bismuth to sequential therapy does not significantly improve Hp eradication success rates. Therefore, Hp eradication is beneficial and necessary in patients with nonulcer dyspepsia.** (Acta gastroenterol. belg., **2017**, 80, **39-42**).

Introduction

Helicobacter pylori (Hp) is the most common chronic bacterial infection in the world and 60% of the global population is infected by Hp (1, 2). Although, Hp infection has high prevalence, most patients infected with Hp are asymptomatic (3). The association between Hp infection with peptic ulcer, atrophic gastritis, gastric lymphoma and gastric cancer has been demonstrated in some studies (4, 5). Altough many patients with functional dyspepsia have been infected by Hp, the benefit of Hp eradication treatment in these patients remains unclear.

The increase in Hp resistance to clarithromycin is the most important cause of the decrease in efficacy of the standard triple therapy. The clarithromycin resistance rate in Europe was 9% in 1998. This rate increased to 17.5% in 2008 (6, 7). On the other hand, in Turkey, clarithromycin resistance rate ranged between 24% and 54.5% (8, 9).

If the clarithromycin resistance rate is high, sequential therapy for 14 days may be more effective than standard triple therapy in eradicating Hp infection (10-15). Moreover, levofloxacin containing sequential therapy may be more cost-effective than clarithromycin containing sequential therapy in areas where clarithromycin resistance is high (16). Because of high prevalence and high drug resistance rates of Hp, more effective and well-tolerated alternative treatment regimens for Hp eradication are needed.

The aim of this study is to determine the efficiency of levofloxacin containing sequential therapy with or without Bismuth, in Hp eradication in nonulcer dyspepsia.

Materials and Methods

Patients who applied to the gastroenterology polyclinic with dyspeptic complaints were evaluated in this study. One hundred and ninety patients who underwent endoscopic biopsy for Hp infection with the pre-diagnosis of nonulcer dyspepsia and who were found positive for Hp infection in biopsy were included in the study.

Age and sex of the patients were recorded. Patients were randomized into 2 groups of 95 individuals. First group was administered levofloxacin containing sequential therapy with bismuth: 2 × 40 mg pantoprazole (14 days), 3 × 300 mg bismuth (14 days), 2 × 1000 mg amoxicillin (first 7 days), 3 × 500 mg metronidazole (second 7 days), and 1 × 500 mg levofloxacin (second 7 days). Second group was administered levofloxacin containing sequential therapy without bismuth: 2 × 40

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mg pantoprazole (14 days), 2 × 1000 mg amoxicillin (first 7 days), 3 × 500 mg metronidazole (second 7 days), and 1 × 500 mg levofloxacin (second 7 days).

Patients were asked to visit the hospital 1 month after termination of therapy for Hp stool antigen test (HpSAT). Ninety-one patients from each group applied for follow-up. The patients were queried regarding whether they completed therapy; if they discontinued therapy, their reasons for discontinuation were also recorded. In addition, the response of patients were recorded after they were asked question regarding whether the therapy was beneficial. Discontinuation rates were compared between the groups.

HpSAT was performed on patients who completed treatment, in both groups. Eradication success rates were compared between the groups. Further, all patients in whom Hp could be and could not be eradicated were evaluated in 2 groups. These 2 groups were compared in terms of benefiting from the therapy and symptomatic healing.

Written informed consent form was obtained from all participants and the protocol was approved by the Non-invasive Clinical Research Ethics Committee of Pamukkale University, Medical Faculty.

Helicobacter pylori stool antigen test technique

A RDS Laboratory Systems, *Helicobacter pylori* Antigen (HP Ag) Test Kit (RDS Laboratory Systems, Ankara, Turkey) was used according to the manufacturer's recommendations. Two band regions (test band and control band) were present on the test device. The test band region was pre-coated with Hp antigens and the control band region was pre-coated with Hp specific monoclonal antibody. If the sample is positive for the Hp specific antibodies, visible color line appears in the test band region. If the sample is negative for the Hp specific antibodies, no visible color line appears in the test band region. The absence of the colored line in the test band region means a negative result.

Statistical Analysis

Descriptive statistics were used for the comparison of data. Chi-square and Student's t-tests were used to compare proportions and means for normally distributed data. A p-value of <0.05 was considered statistically significant. All analyses were performed using SPSS 17.0 version.

Results

Patients were divided into 2 groups such that each group included 95 patients, and they were compared in terms of age and sex. Mean ages of the first and second groups were 44.67±13.43 and 45.11±14.40 years, respectively; there was no statistically significant difference between the groups ($p > 0.05$). There were 57 women (60.6%) in the first group, 55 women (57.9%) in the second group; there was no statistically significant difference in terms of sex between the groups ($p > 0.05$) (Table 1).

Ninety-one patients from each group applied for follow-up after treatment. Four patients from each group did not attend follow-up and were excluded from the study. Seven out of 91 patients (7.6%) from the first group and 5 out of 91 patients (5.4%) from the second group did not complete the Hp eradication therapy. No statistically significant difference was observed in terms of the therapy discontinuation rates between the 2 groups ($p > 0.05$) (Table 2). Four out of 7 patients did not complete therapy in the first group because of gastrointestinal system (GIS) intolerance, and 3 of them failed to take medication regularly. In the second group, 4 out of 5 patients who did not complete therapy because of GIS intolerance, and 1 failed to take medication regularly.

Patients who completed therapy from both groups were compared in terms of post-therapy Hp eradication rates. Hp was eradicated in 72 of 84 patients (85.2%) from the first group and 71 of 86 patients (85.2%) from the second group. No statistically significant difference was observed between the 2 groups in terms of eradication success rates ($p > 0.05$) (Table 2).

Table 1. — **Comparison of age and sex between two groups**

	Group 1 (n=95)	Group 2 (n=95)	P value
Age (years)	44.67±13.43	45.11±14.40	p>0.05
Sex (Female)	57 (60.6%)	55 (57.9%)	p>0.05

Group 1: Sequential treatment with bismuth
Group 2: Sequential treatment without bismuth

Table 2. — **Comparison of discontinuation rates and successful Hp eradication rates of therapies between two groups**

	Group 1	Group 2	P value
Discontinuation rates	7/91 (%7.6)	5/91(%7.6)	p>0.05
Successful eradication rates	72/84 (%85.2)	71/86 (%82.6)	p>0.05

Group 1: Sequential treatment with bismuth
Group 2: Sequential treatment without bismuth

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Table 3. — **Comparison of symptomatic healing rates of dyspeptic patients in whom Hp could be eradicated and couldn't be eradicated**

	Hp could be eradicated patients (n:431)	Hp couldn't be eradicated patients (n:27)	P value
Patients with symptomatic healing	125 (87,4%)	12 (44,4%)	P <0,001

Among the total of 170 patients who completed therapy, 143 had a negative HpSAT and 27 had a positive HpSAT. These patients were evaluated in 2 groups and these groups were compared in terms of the rate of symptomatic healing after therapy completion. Of 143 patients, 125 (87.4%) had symptomatic healing in the group in which Hp was eradicated, and 12 out of 27 patients (44.4%) had symptomatic healing in the group in which Hp was not eradicated. The rate of symptomatic healing in dyspeptic complaints was found to be higher in the group in which Hp was eradicated than in the group in which Hp was not eradicated ($p < 0.001$) (Table 3).

Discussion

In developing countries, where the majority of children are infected by Hp before age 10 years, the prevalence of Hp in adults peaks to more than 80% before age 50 years (17, 18). Testing for and treating Hp may be preferable to a strategy of just prescribing a proton pump inhibitor, in young patients with dyspepsia, where the Hp prevalence is ≥20%. Patients <55 years of age without alarm features should be tested and treated for Hp, if the local prevalence of Hp is >10% (19). Maconi et al. suggested that Hp eradication provides a similar long-term symptomatic healing, in patients with nonulcer dyspepsia and peptic ulcus (20).

In our study, symptomatic healing rate was markedly superior in the group in which Hp was eradicated than in the group in which Hp was not eradicated ($p < 0.001$). On the basis of this data, Hp eradication may be considered effective on symptomatic healing in patients with nonulcer dyspepsia.

However Hp resistance to clarithromycin is increasing in Europe and Turkey (6-9). Hence, more effective and well-tolerated alternative treatment regimens to standard triple therapy are needed.

In areas where the prevalence of clarithromycin or metronidazole resistance rate is ≥15%, quadruple therapy may be a suitable choice as initial therapy (21). In treatment-naïve patients with Hp, it has been demonstrated that sequential therapy and concomitant quadruple therapy are equally effective on eradication rates (22-24). Moayyedi et al. suggested that levofloxacin (250 mg twice daily) may be used in patients with penicillin allergy or in areas where clarithromycin resistance rate is >15% (10).

Romano et al. compared clarithromycin containing sequential therapy for 10 days with levofloxacin containing sequential therapy (250 mg and 500 mg twice daily). Eradication rates were significantly higher in groups with both levofloxacin containing sequential therapy than the group with clarithromycin containing sequential therapy (96, 97, and 81 percent, respectively) (16).

In our study, we demonstrated that levofloxacin containing sequential therapy is quite effective and well tolerated for Hp eradication. However, adding bismuth to levofloxacin containing sequential therapy does not significantly improve Hp eradication success rates. On the other hand, adding bismuth to therapy does not increase therapy discontinuation rates.

In summary levofloxacin containing sequential therapy for 14 days is quite effective and well-tolerated choice for Hp eradication. Adding bismuth to therapy leads to no difference in terms of side effects and discontinuation of therapy. However, adding bismuth to levofloxacin containing sequential therapy does not significantly improve Hp eradication success rates. Nevertheless, Hp eradication provides significant improvement in symptoms in nonulcer dyspepsia. Therefore, Hp eradication is beneficial and necessary in patients with nonulcer dyspepsia.

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