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EVALUATION OF THE EFFICACY OF TWO DIFFERENT HELIOCOBACTER PYLORI ERADICATION REGIMENS AT A SECONDARY PUBLIC HEALTH CARE CENTER

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ABSTRACT

Objective: Helicobacter pylori (H. pylori) is a bacterium that infects more than half of the world's population and is defined as a class 1 carcinogen by the World Health Organization. The aim of this study is to compare the efficacy of treatments in patients with H. pylori positivity who were treated with a modified sequential treatment regimen containing levofloxacin or a bismuth-based quadruple treatment regimen in a secondary state hospital.
Method: This study includes retrospective analysis of 167 patients who received and tolerated H. pylori eradication therapy between April 2021 and April 2022. The patients included in the study were divided into two groups according to the treatment regimen they received. Patients given a modified sequential treatment regimen containing levofloxacin (amoxicillin 1 g 2x1, pantoprazole 40 mg 2x1 for 7 days, followed by pantoprazole 40 mg 2x1 for 7 days, metronidazole 500 mg 3x1, levofloxacin 500 mg 1x1) Group 1 and the patients who were given bismuth-based quadruple therapy (14 days pantoprazole 40 mg 2x1, bismuth subsalicylate 262 mg 2x2, metronidazole 500 mg 3x1 and tetracycline 500 mg 4x1) were determined as Group 2.
Results: A total of 14 patients (one in group 1 and 13 in group 2) could not tolerate H.pylori treatment, and eradication was achieved in 83 (90.2%) in group 1 and 70 (93.3%) in group 2 of 167 patients who completed the treatment. There was no statistically significant difference in eradication success rates in both treatment protocols (p=.470). There was no significant difference between the treatment groups in terms of age, gender, indications for endoscopy, endoscopic diagnoses, pathological findings, and eradication indications.
Conclusion: Considering the eradication success rates found in our study, it supports that the modified sequential treatment regimen containing levofloxacin may be an alternative to bismuth-based treatment in the first-line treatment in our country, or a second-line treatment in patients who cannot tolerate bismuth-based treatment. However, further studies on modified sequential therapy containing levofloxacin are needed.

Key Words: Bismuth, eradication, Helicobacter pylori, levofloxacin.

1. INTRODUCTION

Helicobacter pylori (H. pylori) is a bacterium that has infected at least half the world's population, has a high prevalence in developing countries, and has been classified as a class 1 carcinogen by the World Health Organization [1,2]. In infected individuals, it colonizes the gastric mucosa and remains usually asymptomatic [3,4]. H. pylori selectively colonizes the gastric mucosa and is involved in the development of chronic active gastritis, atrophic gastritis, intestinal metaplasia, dysplasia, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma (MALT lymphoma) [5-7].

Diagnosis may be established using invasive tests such as culture, histopathology, rapid urease test, and polymerase chain reaction as well as non-invasive tests such as stool antigen test and urea breath test [8]. In infected individuals, H. pylori eradication can prevent recurrence of peptic ulcer, treat low-grade MALT lymphoma, and prevent precancerous lesions from evolving into adenocarcinoma [9-11]. This makes H. pylori eradication therapy all the more important. The most common antibiotics used in H. pylori eradication therapy include clarithromycin, metronidazole, amoxicillin, tetracycline, and levofloxacin. Increasing antibiotic resistance has led to a decline in eradication rates in recent years and prompted a

search for new treatment regimens [12,13]. In countries with clarithromycin resistance rates >15% such as Turkey, modified sequential treatment regimen containing levofloxacin and bismuth-based quadruple therapy have been put forward as the first two treatment options [14].

This study aimed to compare the efficacy of modified sequential treatment regimen containing levofloxacin with bismuth-based quadruple therapy in patients who underwent upper gastrointestinal tract (GI) endoscopy for any indication at a secondary public hospital and were found to be infected with H. pylori.

2. MATERIALS AND METHODS

This study is a retrospective analysis of 167 patients who underwent upper GI endoscopy at the Endoscopy Unit of Burdur Public Hospital between April 2021 and April 2022, who were found to be infected with H. pylori according to the pathology report after endoscopic biopsy, and who received and tolerated H. pylori eradication therapy.

Upper GI endoscopy data of the patients were extracted from the database of the endoscopy unit. Age, sex, reason for endoscopy, and endoscopic diagnosis were recorded from the patients' upper GI reports. Data on the presence of H. pylori and pathologic diagnosis were extracted from the pathology reports available in the hospital's electronic database. Hospital electronic outpatient clinic files were reviewed for H. pylori eradication status based on the stool H. pylori antigen test as well as patients' reports of side effects related to the use of medications and completion or discontinuation of treatment.

All patients scheduled for upper GI endoscopy were advised to fast for 8 hours before the procedure. Written informed consent was obtained from all patients. The patients received 10% lidocaine spray (Xylocaine 10% spray; Astra Zeneca, Sweden) for pharyngeal topical anesthesia and intravenous midazolam (Dormicum; Roche, Switzerland) for sedation. Upper GI endoscopic examinations were performed by a gastroenterologist and an endoscopy nurse using EG 530WR; Fujinon device (Tokyo, Japan). During the upper GI endoscopy, at least two biopsies were collected from each of the antrum and corpus. The presence of H. pylori was detected using gastric mucosa biopsy slides stained with hemotoxylin eosin and giemsa and were examined under light microscopy.

The patients were divided into two groups based on the treatment regimen: Group 1 consisted of patients who received modified sequential treatment regimen containing levofloxacin (amoxicillin 1 g 2×1 and pantoprazole 40 mg 2×1 for 7 days, followed by pantoprazole 40 mg 2×1, metronidazole 500 mg 3×1, and levofloxacin 500 mg 1×1 for 7 days) and Group 2 consisted of patients who received bismuth-based quadruple therapy (14 days of pantoprazole 40 mg 2×1, bismuth subsalicylate 262 mg 2×2, metronidazole 500 mg 3×1, and tetracycline 500 mg 4×1). Four weeks after the treatment, stool samples were collected from the patients to examine the efficacy of eradication using a qualitative immunochromatography-based stool antigen test (Guangzhou Wondfo Biotech, China) with monoclonal antibodies to detect H. pylori proteins in the stool.

Patients were excluded if they were younger than 18 years of age, had gastric adenocarcinoma or chronic kidney damage, had used proton pump inhibitors, antibiotics and/or bismuth compounds over the last two weeks, had any condition that was a contraindication for any of the drugs included in the eradication protocol, were pregnant or breastfeeding, or discontinued the medication therapy due to side effects during eradication treatment.

2.1. Ethical Approval

Our study received ethics committee approval (ethics committee approval date/no: 01.06.2022/22-5.1T/13) and was conducted in accordance with the principles of the Declaration of Helsinki.

2.2. Statistical Analysis

The normality of distribution for the age variable was checked using visual (histogram) and analytical

Table 1. Comparison of demographic, clinical, endoscopic, and pathologic characteristics of the patients .

	Group 1 n(%)	Group 2 n(%)	p
Age (years, Mean ± SD)	49.14±14.9	53.2±13.34	0.069
Sex			
Female	62(67.4)	42(56)	0.131
Male	30(32.6)	33(44)	
Indications for endoscopy			
Dyspepsia	53(57.6)	49(65.3)	
Atrophy/intestinal metaplasia follow-up	8(8.7)	6(8)	
Dyspepsia + iron deficiency anemia	3(3.3)	5(6.7)	
Family history of stomach cancer + dyspepsia	5(5.4)	3(4)	0.525
Other*	23(25)	12(16)	
Endoscopic diagnosis			
Endoscopic erythematous pangastritis	56(60.9)	47(62.7)	
Endoscopic atrophic gastritis	16(17.4)	17(22.7)	
Endoscopic erythematous pangastritis + gastric polyp	7(7.6)	3(4)	0.488
Stomach ulcer	3(3.3)	4(5.3)	
Other**	10(10.8)	4(5.3)	
Pathological findings			
Atrophy of the antrum	30(32.6)	20(26.7)	
Chronic gastritis	20(21.7)	19(25.3)	
Atrophy of the antrum and corpus	20(21.7)	22(29.4)	
Atrophy of the antrum + intestinal metaplasia	4(4.3)	7(9.3)	0.191
Other***	18(19.6)	7(9.3)	
Indications for eradication			
Presence of atrophy and/or intestinal metaplasia	66(71.7)	54(72)	
Dyspepsia and patient's request	15(16.3)	12(16)	
Family history of gastric cancer and gastric atrophy	5(5.4)	4(5.3)	1.000
Stomach ulcer	4(4.4)	3(4)	
Bulbus ulcer	2(2.2)	2(2.7)	

Group 1: Modified sequential treatment regimen containing levofloxacin, **Group 2:** Bismuth-based quadruple therapy.

*Iron deficiency anemia (n = 8), dysphagia (n = 7), treatment-resistant nausea and vomiting (n = 5), family history of gastric cancer + iron deficiency anemia (n = 6), dyspepsia + weight loss (n = 4), melena (n = 3), iron deficiency anemia + vitamin B12 deficiency (n = 1), increased antrum wall thickness on ultrasonography and dyspepsia (n = 1).

**Endoscopic atrophic gastritis + intestinal metaplasia (n = 6), bulbus ulcer (n = 4), endoscopic erosive antral gastritis (n = 2), erythematous pangastritis + hiatus hernia (n = 1), gastric ulcer + hiatus hernia (n=1).

***Atrophy in the antrum and corpus + intestinal metaplasia (n = 10), atrophy in the antrum + hyperplastic polyp (n = 8), ulcer (n = 5), atrophy in the antrum + fundic gland polyp (n = 2).

Table 2. H. pylori eradication in patients who completed the treatment

	Group 1 n(%)	Group 2 n(%)	All patients n(%)	p
H.pylori eradication	92(100)	75(100)	167(100)	
Successful	83(90.2)	70(93.3)	153(91.6)	0.470
Failed	9(9.8)	5(6.7)	14(8.4)	

Group 1: Modified sequential treatment regimen containing levofloxacin, **Group 2:** Bismuth-based quadruple therapy.

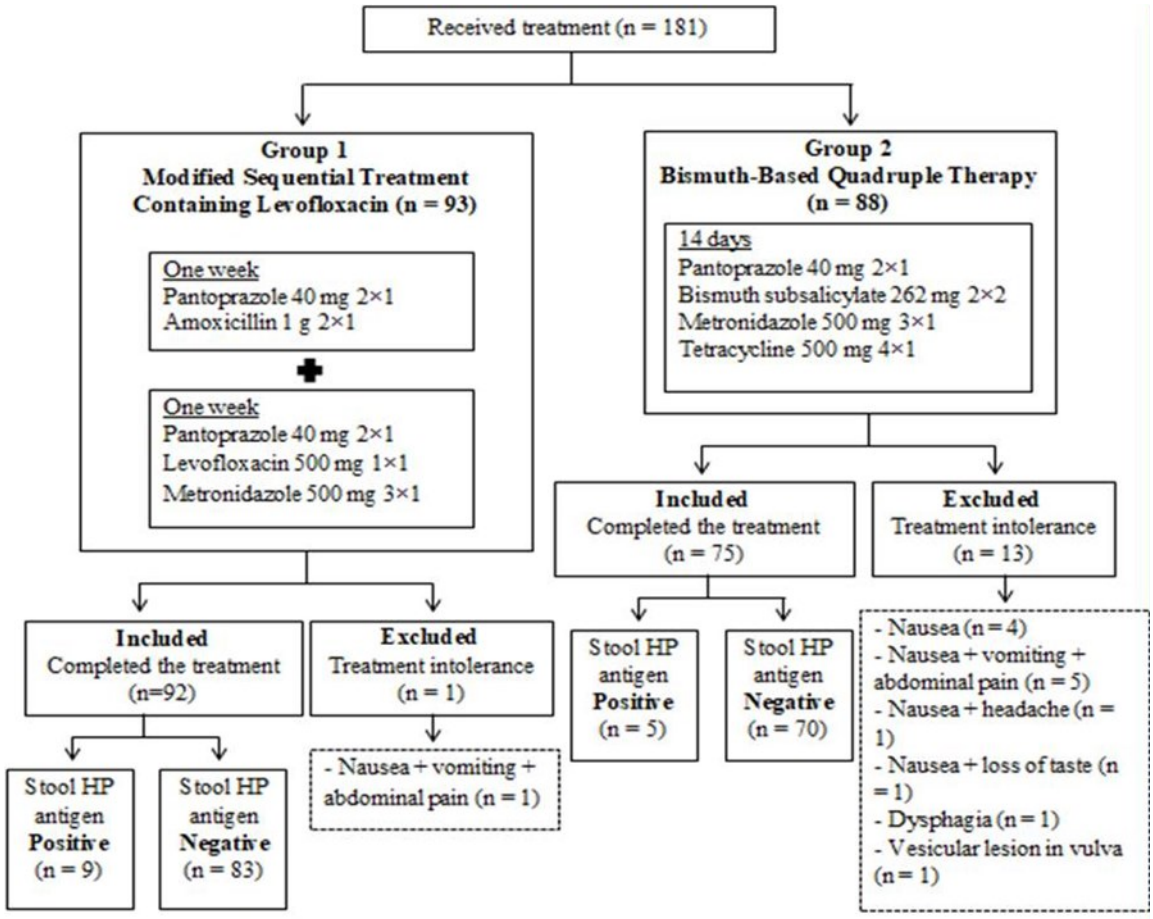

Figure 1. . Flow chart of the study

methods (Kolmogorov–Smirnov test). The age variable was expressed in mean, median, standard deviation, and maximum–minimum value, while categorical data was expressed using descriptive methods such as rate and percentage. Inter-group comparisons were performed using the Student's t-test for the age variable and the Chi-square test for categorical variables. P values <.05 were considered statistically significant. All statistical analyses and calculations were performed using SPSS Statistics Ver. 22.0.

3. RESULT AND DISCUSSION

Out of 181 patients who received H. pylori eradication therapy, 167 patients tolerated and completed the therapy and were retrospectively analyzed. Ninety four (51.4%) patients received modified sequential treatment regimen containing levofloxacin (Group 1) and 88 (48.6%) patients received bismuth-based quadruple therapy (Group 2). One (1.1%) patient from Group 1 and 13 (14.8%) patients from Group 2, 14 patients in total, could not tolerate the treatment and were excluded from the study (Figure 1).

Out of the patients included in the study, 104 (62.2%) were female with mean age 50.6 years (min:18, max:78). There was no difference between Group 1 and Group 2 in terms of age and sex. The most common indication for upper GI endoscopy in the treatment groups was dyspepsia, with no statistically significant difference between the groups in terms of indications for endoscopy (p=.525). The most common findings on upper GI endoscopy in Group 1 and 2 were endoscopic erythematous pangastritis and endoscopic atrophic gastritis, respectively, with no statistical difference between the two groups (p=.488). The most common pathologic findings in both groups were atrophy of the antrum, chronic gastritis, and atrophy of the antrum and corpus, with no significant difference between the groups (p=.191). The most common indication of H. pylori in both groups was the presence of atrophy and/or intestinal metaplasia, with no statistically significant difference between the groups (p=1.000) (Table 1).

Analysis of post-treatment H. pylori eradication rates in 167 patients who completed the treatment showed that eradication was achieved in 83 (90.2%) patients in Group 1 and 70 (93.3%) patients in Group 2. The treatment protocols had no statistically significant difference in terms of eradication success rates (p=.470) (Table 2).

It is known that at least half the world's population is infected with H. pylori, with infection rates of 70%–90% in developing countries and 25%–50% in developed countries [15]. Even within the same country, H.pylori prevalence may vary between regions. Clarithromycin resistant H. pylori is around 40% in Turkey and this has prompted searches for alternative agents [14]. Although there is no consensus on treatment in Turkey, the most widely used options seem to be bismuth-based therapy and levofloxacin-containing therapy. Against this background, this study aimed to retrospectively evaluate the eradication success of both treatment regimens used in our clinic, located in the Mediterranean region of Turkey.

Previous studies have reported that bismuth-based therapies obtained per-protocol eradication rates of 80.4%–97.1% [16-21]. Studies from different geographical regions in Turkey, on the other hand, have found bismuth-based therapies to achieve H. pylori eradication rates of 66.7%–92.3% [22-25]. In our study, the eradication rate with bismuth-based therapy was 93.3%, which is in line with previous studies from both Turkey and other countries.

Modified sequential treatment regimens containing levofloxacin have been reported to obtain eradication rates of 85%–90.2% in the intention-to-treat (ITT) analysis and 87.6%–91.4% in PP analysis [26,27]. Romano et al. and Molino-Infante et al. reported an eradication rate of 95% and 82.5%, respectively [28,29]. In Turkey, Aydın A et al. found modified sequential treatment regimens containing levofloxacin to result in eradication rates of 80% in ITT and 84.2% in PP analysis [30]. Other studies from Turkey have reported eradication rates with modified sequential treatment containing levofloxacin to be 90%–94.5% in PP analysis [31,32]. Our study, found an eradication rate of 90.2%, which is in line with previous studies.

Our study achieved high eradication rates in both treatment groups; these results confirm the utility of bismuth-based therapies as a first-line treatment in Turkey, where clarithromycin resistance rate is around 40%, as recommended in the literature. Furthermore, based on the successful eradication of H. pylori with modified sequential treatment regimen containing levofloxacin in our region, our results add to the potential value of this treatment regimen as another good option for first-line treatment in Turkey.

Previous studies have reported that 5%–30% of patients receiving bismuth-based therapy discontinue it due to side effects. The most commonly reported side effects are diarrhea, nausea, and vomiting [33-35]. Due to the side effect profile and the high number of medications administered in bismuth-based therapy, patients discontinue the treatment and/or skip doses. In our study, 14.8% of the patients discontinued the

treatment due to side effects and were excluded from the analysis, which is consistent with the literature. The most common side effects causing our patients to discontinue the therapy were nausea, vomiting, and abdominal pain. As for modified sequential treatment containing levofloxacin, there is insufficient data on discontinuation of therapy; a study conducted by Chuah SK et al. with 82 patients reported a completion rate of 98.8% with only one patient failing to complete the treatment due to headache and nausea [26]. Likewise, in our study, one patient failed to complete the treatment due to nausea and vomiting. Figure 1 shows patients and their reasons for discontinuation of treatment.

Our study has some limitations: the study had a retrospective and single-centered design, patient population was small and came from a limited region, data on smoking and alcohol use was not available, data on chronic diseases could not be accessed, and response to treatment was evaluated using a single method. Furthermore, since our study was retrospective, statistical analysis of the treatment protocols could not use ITT and PP methods.

4. CONCLUSION

The eradication rates and side effect profiles found in our study support the hypothesis that the modified sequential treatment regimen containing levofloxacin can be an alternative to bismuth-based therapy as a first-line treatment or can be a second-line treatment in patients who cannot tolerate bismuth-based therapy in Turkey. However, further investigations on fluoroquinolone resistant H. pylori in Turkey and on modified sequential treatment regimens containing levofloxacin are required.

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Conflict of interest: The authors declared that there is no conflict of interest.

Ethical Approval: Local ethics committee approval was obtained for the study (ethics committee approval date/no: 01.06.2022/22-5.1T/13).

REFERENCES

1. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet. 1984;1:1311-5.

2. Lawson AJ. Helicobacter. In: Jorgensen JH, Landry ML, Warnock DW, eds. Manual of Clinical Microbiology. Washington DC: ASM Press; 2011:900-15.

3. Goh KL, Chan WK, Shiota S, Yamaoka Y. Epidemiology of Helicobacter pylori infection and public health implications. Helicobacter. 2011;16Suppl 1(01):1–9.

4. Eusebi LH, Zagari RM, Bazzoli F. Epidemiology of Helicobacter pylori infection. Helicobacter. 2014;19 Suppl 1:1–5

5.Brown LM. Helicobacter pylori: epidemiology and routes of transmission. Epidemiol Rev. 2000;22(3):283-97

6. Craanen ME, Dekker W, Blok P, Ferwerda J, Tytgat GN. Intestinal metaplasia and Helicobacter pylori: an endoscopic bioptic study of the gastric antrum. Gut. 1992;33:16-20.

7.Weck MN, Brenner H. Association of Helicobacter pylori infection with chronic atrophic gastritis: Meta-analyses according to type of disease definition. Int J Cancer. 2008;123:874-81.

8. Megraud F, Lehours P. Helicobacter pylori detection and antibiotic susceptibility testing. Clin Microbiol Rev. 2007;20(2):280-322.

9. Shimoyama T. Stool antigen tests for the management of Helicobacter pylori infection. World J Gastroenterol. 2013;19 (45):8188-91.

10. Tomita T, Fukuda Y, Tamura K, et al. Successful eradication of Helicobacter pylori prevents relapse of peptic ulcer disease. Aliment Pharmacol Ther. 2002;16 (Suppl 2):204-9.

11.Zullo A, Hassan C, Cristofari F, Perri F, Morini S. Gastric low-grade mucosal-associated lymphoid tissue-lymphoma: Helicobacter pylori and beyond. World J Gastrointest Oncol. 2010;2(2):181-6.

12. Bazzoli F, Bianchi Porro G, Bianchi MG, Molteni M, Pazzato P, Zagari RM. Treatment of Helicobacter pylori infection. Indications and regimens: an update. Dig Liver Dis. 2002 Jan;34(1):70-83.

13. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. 2017;112(2):212–38.

14.Malfertheiner P, Megraud F, O'Morain CA, et al. Management of Helicobacter pylori infection-the Maastricht V/Florence Consensus Report. Gut. 2017;66(1):6-30.

15. Dunn BE, Cohen H, Blaser MJ. Helicobacter pylori. Clin Microbiol Rev. 1997;10(4):720-41.

16. Gatta L, Vakil N, Vaira D, Scarpignato C. Global eradication rates for Helicobacter pylori infection: systematic review and meta -analysis of sequential therapy. BMJ. 2013;347:f4587.

17.Li B-Z, Threapleton DE, Wang J-Y, et al. Comparative effectiveness and tolerance of treatments for Helicobacter pylori: systematic review and network meta-analysis. BMJ. 2015;351:h4052.

18. Liou J-M, Chen C-C, Fang Y-J, et al. 14-day sequential therapy versus 10-day bismuth quadruple therapy containing high-dose esomeprazole in the first-line and second-line treatment of Helicobacter pylori: a multicentre, non-inferiority, randomized trial. J Antimicrob Chemother. 2018;73(9):2510-8.

19. Tsay F-W, Wu D-C, Yu H-C, et al. Both 14-day hybrid and bismuth quadruple therapies cure most patients with

Helicobacter pylori infection in populations with moderate antibiotic resistance: a randomized controlled trial. Antimicrob Agents Chemother. 2017;61(11):e00140-17.

20. Salazar CO, Cardenas VM, Reddy RK, Dominguez DC, Snyder LK, Graham DY. Greater than 95% success with 14-day bismuth quadruple anti- Helicobacter pylori therapy: a pilot study in US Hispanics. Helicobacter. 2012;17(5):382-90.

21. Seo SI, Lim H, Bang CS, et al. Bismuth-based quadruple therapy versus metronidazole-intensified triple therapy as a first-line treatment for clarithromycin-resistant Helicobacter pylori Infection: A multicenter randomized controlled trial. Gut Liver. 2022;16(5):697-705.

22. Nazım EK, Berat EB, Bacaksız F. Evaluation of the efficacy of three different treatment regimens in patients receiving Helicobacter Pylori first-line treatment. Journal of Harran University Medical Faculty. 2021;18(1):100-3.

23. Aydemir S, Bayraktaroğlu T, Üstündağ Y, et al. The efficacy of quadruple therapy consisting of lansoprazole, ranitidine bismuth citrate, tetracycline and metronidazole in Helicobacter pylori infection not eradicated with standard triple therapy. Journal of Academic Gastroenterology. 2004;3(3):129-33.

24. Uygun A, Kadayifci A, Safali M, Ilgan S, Bagci S. The efficacy of bismuth containing quadruple therapy as a first-line treatment option for Helicobacter pylori. J Dig Dis. 2007;8(4):211-5.

25. Özden A, Seven G, Bektaş M. Effectiveness of different treatment regimens in helicobacter pylori eradication: Tenyear experience of a single institution. Turk J Gastroenterol. 2010;21 (3):218–23.

26. Chuah SK, Liang CM, Lee CH, et al. A randomized control trial comparing 2 levofloxacin-containing second-line therapies for Helicobacter pylori eradication. Medicine (Baltimore). 2016;95 (19):e3586.

27. Sherkatolabbasieh H, Shafizadeh S, Azadbakht S, et al. Levofloxacin-based sequential therapy versus classic triple therapy in Helicobacter pylori eradication: A randomized clinical trial. Biomedical Research and Therapy. 2017;4(11):1785-94.

28. Romano M, Cuomo A, Gravina AG, et al. Empirical levofloxacin-containing versus clarithromycin-containing sequential therapy for Helicobacter pylori eradication: a randomized trial. Gut. 2010;59:1465–70.

29. Molina-Infante J, Perez-Gallardo B, Fernandez-Bermejo M, et al. Clinical trial: clarithromycin vs. levofloxacin in first-line triple and sequential regimens for Helicobacter pylori eradication. Aliment Pharmacol Ther. 2010;31:1077–84.

30. Aydin A, Oruc N, Turan I, Ozutemiz O, Tuncyurek M, Musoglu A. The modified sequential treatment regimen containing levofloxacin for Helicobacter pylori eradication in Turkey. Helicobacter. 2009;14(6):520-4.

31. Ozdil K, Calhan T, Sahin A, et al. Levofloxacin based sequential and triple therapy compared with standard plus probiotic combination for Helicobacter pylori eradication. Hepatogastroenterology. 2011;58(109):1148-52.

32. Polat Z, Kadayifci A, Kantarcioglu M, Ozcan A, Emer O, Uygun A. Comparison of levofloxacin-containing sequential and standard triple therapies for the eradication of Helicobacter pylori. Eur J Intern Med. 2012;23(2):165-8.

33. Nyssen OP, Perez-Aisa A, Tepes B, et al; Hp-EuReg Investigators. adverse event profile during the treatment of Helicobacter pylori: a real-world experience of 22,000 patients from the European Registry on H. pylori management (Hp-EuReg). Am J Gastroenterol. 2021;116(6):1220-9.

34. Losurdo G, Cubisino R, Barone M, et al. Probiotic monotherapy and Helicobacter pylori eradication: A systematic review with pooled-data analysis. World J Gastroenterol. 2018;24(1):139-49.

35. Chung JW, Lee JH, Jung HY, et al. Second-line Helicobacter pylori eradication: a randomized comparison of 1-week or 2-week bismuth-containing quadruple therapy. Helicobacter. 2011;16 (4):289-94.