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Comparison of Clarithromycin and Levofloxacin-Based Regimens as First Line Triple Therapy in Eradication of Helicobacter Pylori Infection

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Abstract

Background: Helicobacter pylori (H. pylori) is the most prevalent chronic bacterial infection and is associated with peptic ulcer disease, chronic gastritis, gastric adenocarcinoma, and gastric mucosa associated lymphoid tissue (MALT) lymphoma.

Aim: The aim of this study was evaluation the efficacy and safety of the eradication of helicbacter pylori infections based on the two treatments, clarithromycin and levofloxacin based as first-line therapy.

Material and Methods: This retrospective, two center, comparative, observational study was conducted at University Clinical Centre in Kosovo, at the Clinic of Gastroenterology and Hepatology and in "Gastro" Clinic Center, between January 2017 and December 2019. Patients diagnosed with H. pylori infection and treated with levofloxacin triple therapy or clarithromycin-based regimen for 10 days were included. In total, 250 patients were divided randomly into two groups. In the first group, 120 patients are treated with PLA (Pantoprazole tab 40 mg, Levofloxacin tab 500 mg and Amoxicillin tab 1000 mg), all twice daily, for 10 days.

Results: Helicobacter pylori infection in PLA group, was cured in 102 of the 120 patients, and in PCA (PPI-clarithromycin-amoxicillin) group cured were achieved in 105 of the 130 patients, who returned for follow-up. Eradication rates were 85% (95% CI (confidence interval): 84.1–85.9) by intention-to-treat analysis and 87% (95% CI: 86.2–87.8) per protocol for therapy and 80% (95% CI: 79.1–81.6) by intention-to-treat analysis and 83% (95% CI: 83–83.7) per protocol for PCA therapy. Factors influencing the efficacy of therapy were analysed; there were no statistical differences regarding indication for treatment, ulcer location, gender, age, smoking habit, or comorbidity.

Conclusions: In conclusion, this 10-day triple therapy combining PPI with high-dose amoxicillin and Levofloxacin two times a day is approximately well tolerated and seems effective in eradicating H. pylori as standard triple therapy in the first line.

Keywords: Eradication; Antibiotics; Tripple Therapy; Helicobacter Pylori.

Introduction

Helicobacter pylori (H. pylori) is the most prevalent chronic bacterial infection and is associated with peptic ulcer disease, chronic gastritis, gastric adenocarcinoma, and gastric mucosa associated lymphoid tissue (MALT) lymphoma [1-4]. Because Helicobacter pylori has been known to cause cancer since 1994, eliminating H pylori reduces the risk of recurrent peptic ulcer disorders and prevents stomach cancer [5]. Clarithromycin triple therapy, which consists of two daily doses of clarithromycin, amoxicillin, and a PPI, is one of the most often used first-line regimens. Treatment for 10-14 days is advised since it may be more successful at treating infections over a longer period of time [6-8]. Metronidazole can be used instead of amoxicillin in penicillin-allergic individuals. PPI-clarithromycin-metronidazole and PPI-clarithromycin-amoxicillin regimens are equivalent [2,10]. The choice of initial antibiotic regimen to treat H. pylori should be guided by the presence of risk factors for macrolide resistance and the presence of a penicillin allergy [6]. Patients who have one or more macrolide resistance risk factors should not get clarithromycin-based treatment. When selecting an alternative empirical antibiotic treatment for H. pylori, a resistance threshold of ≥15 % is frequently employed [2,7].

In China, primary resistance of H. pylori to clarithromycin, metronidazol, and levofloxacin is high and has increased over time (28.9%, 63.8%, and 28.0%, respectively) [10]. Levofloxacin triple therapy consists of levofloxacin, amoxicillin, and a PPI for 10 to 14 days. In a network, meta-analysis eradication rates with levofloxacin triple therapy for 10 to 14 days were significantly higher than clarithromycin triple therapy for seven days (90 versus 73 percent) [11]. Although not directly compared, the pooled eradication rate of levofloxacin triple therapy was also higher than clarithromycin triple therapy for 10 to 14 days (81 percent, 95% CI, 78 to 84 percent) [11]. For people who are allergic to penicillins, metronidazole can be used in place of amoxicillin. Levofloxacin has been used as a first-line antibiotic treatment in numerous investigations. It has been noted that replacement from clarithromycin to levofloxacin improves H. pylori eradication rates [13,14].

Eradication rates in some of these studies range from 85% to 92%, which is an outstanding result. Furthermore, levofloxacin has a strong safety record and is said to have fewer adverse effects [15]. However, validation of the efficacy of levofloxacin-based treatment as the first-line treatment is required before its clinical application in different countries.

Objective

Therefore, we aimed to assess the eradication rates of the two treatments, clarithromycin and levofloxacin based as first-line eradication triple therapies.

Materials and Methods

This research is comparative, observational study was conducted in centres at University Clinical Centre in Kosovo at the Clinic of Gastroenterology and Hepatology and in “Gastro” Clinic Center, between January 2017 and December 2019.

For each endoscopic examination, written consent is obtained for to the procedure. We do not have a decision from the ethics committee because this is retrospective research.

Patients diagnosed with H. pylori infection and treated with levofloxacin triple therapy or clarithromycin-based regimen for 10 days were included. Patients were excluded if: previous H. pylori treatment (last 6 months), previous gastric surgery, severe systemic illness (such as liver cirrhosis or kidney failure), allergy to any of the antibiotics used, pregnancy, and age lower than 18 years. All patients with a personal history for peptic ulcer disease, gastritis, with a family history of gastric cancer and dyspeptic symptoms that didn’t respond to PPI for at least two months, were included consecutively. As a country in development, probably we have a high prevalence of H. pylori infection. For this reason, H. pylori infection at entry was determined by two out three of the following positive tests: Urea breath test, Stool antigen assay and Serology test or a positive Biopsy urease test on Endoscopic testing. Patients are considered positive for H. pylori when two tests resulted positive or with a positive biopsy urease test.

In total, 250 patients were divided randomly into two groups. In the first group, 120 patients are treated with Pantoprazole tab 40 mg, Levofloxacin tab 500 mg and Amoxicillin tab 1000 mg, all twice daily (PLA group), for 10 days. In the second group, 130 patients, are treated with Pantoprazole tab 40 mg, Clarithromycin tab 500 mg and Amoxicillin tab 1000 mg, all twice daily (PCA group), for 10 days. Eradication was mainly evaluated with a Urea breath test, Stool antigen assay, except for a few patients with gastric ulcer, who underwent a second endoscopy to rule out gastric cancer. In this case, eradication was assessed by histology, for the confirmed benign or malign aspect in same time. The diagnostic test was performed at least 8 weeks after treatment. Although patients were allowed to use PPI in case of dyspepsia, they were instructed to avoid PPI for at least 2 weeks before the diagnostic test. Therapy compliance and adverse events were assessed at follow-up the after the treatment. We considered good compliance when the patient reported taking more than 80% of the tablets.

Statistical analysis. The overall eradication rates and their 95% Ci (confidence interval) were obtained by intention-to-treat and per protocol. Quantitative variables were given as mean, ± s.d (standard deviation). A univariate analysis including age (divided into quartiles), gender, smoking habit (active smoker vs. non-smoker), comorbidity and indication for treatment (ulcer vs. non-ulcer) was performed using the $\chi 2$ test or the Mann–Whitney U-test. An expected intention-to-treat cure rate of 90% was assumed. A sample of 250 patients was necessary to obtain an estimation of the efficacy of the treatment with a ±5% error margin and a 95% CI. Was evaluated efficacy of two regimens, their adverse effects. Results are presented with respective tables and graphics with statistically analysis.

Results

Two hundred and fifty patients, divided in two consecutive groups (PLA group and PCA group) were included in the study. Demographic and clinical characteristics and the indications for eradication are shown in Table 1. The diagnosis of H. pylori infection was confirmed by at least two out of three positive following tests: Urea breath test, Stool antigen assay and Serology test or a positive Biopsy urease test on Endoscopic testing. Sixty per cent of the patients were men and mean age was 52.6 ± 16 years.

Indications for treatment were: non-investigated dyspepsia and functional dyspepsia (39.6%), gastroduodenal ulcer 15.6%, endoscopic gastritis 33.6% and erosive duodenitis (11.2%).

Helicobacter pylori infection in PLA group, was cured in 102 of the 120 patients, and in PCA group cured were achieved in 105 of the 130 patients, who returned for follow-up.

Eradication rates were 85% (95% CI: 84.1–85.9) by intention-to-treat analysis and 87% (95% Confidence interval (CI): 86.2–87.8) per protocol for PLA therapy and 80% (95% CI: 79.1–81.6) by intention-to-treat analysis and 83% (95% CI: 83–83.7) per protocol for PCA therapy. Factors influencing the efficacy of therapy were analysed; there were no statistical differences regarding indication for treatment, ulcer location, gender, age, smoking habit, or comorbidity (Table 2).

More than 95% of the patients reported complete adherence to treatment. The treatment was well tolerated: no major side effects were reported and no patient dropped out due to adverse events. Only nine patients (6.6%) presented minor-to-moderate side effects (six patients reported metallic taste, six mild diarrhoea and five occasional nausea). All side effects disappeared shortly after the end of treatment.

There were no significant differences in cure between the different triple therapy, as the first line treatment of h. pylori infection in the symptomatic patients.

Characteristics	PLA group	PCA group
Nr. of pt.	120	130
Age (mean ± s.d.)	55-10.8	54-12.2
Male/Female	55/65	72/58
Use of NSAIDs	10	13
Alcohol use	22	28
Smoking	35	38
Endoscopic gastritis	43	41
Gastroduodenal ulcer	17	22
Functional dyspepsia	47	52
Erosive duodenitis	13	15
Prior H. pylori treatment	**No**	**No**

Table 1: Demographic and endoscopic characteristics in both groups.

Adverse events	PLA group	PCA group
Epigastric pain	3	4
Nausea	2	3
Vomiting	3	3
Skin rush	1	1
Diarrhea	2	3
Headache	1	2
Metallic taste	1	1

Table 2: Adverse events in PLA and PCA groups.

Discussion

The most significant finding of this study was that levofloxacin-based first-line therapy and standard triple-therapy for previously untreated H. pylori-infected patients achieved equivalent outcomes. The overall eradication rates were 85% for levofloxacin-based regimens and 80.8% for standard therapy. The overall adverse events were similar between these two regimens. Duration of the treatment and medications used in the levofloxacin based first line therapy and standard therapy were similar.

For more than 20 years, individual studies were published examining treatment of H. pylori with levofloxacin-based first-line therapy. The results of these individual studies support the concept that the efficacy and safety of levofloxacin-based first-line therapy is equivalent to standard first-line therapy.

Levofloxacin-based triple therapy is advised as a second-line treatment for H pylori infections by the Maastricht IV/Florence Consensus Report [2], the American College of Gastroenterology Guideline on the management of H pylori [6], and the Second Asia–Pacific Consensus Guidelines for H pylori infection [9].

Can or no that we recommend levofloxacin-based triple therapy as first-line therapies for H. pylori eradication? Our study suggests that levofloxacin-based triple therapy is as effective as standard therapy for H pylori eradication, and the adverse events and dropout rates are also equal. Noticeably, the overall eradication rates for H pylori with both levofloxacin-based regimens and standard therapy were around 82%. An initial attempt to eradicate H. pylori is unsuccessful in about 20% of patients [12].

According to data, antibiotic resistance in H. pylori is widespread. Primary and secondary resistance to clarithromycin, metronidazole, and levofloxacin were high (≥15 \%) in most WHO areas, according to a comprehensive review and meta-analysis that included 178 studies and 66,142 isolates from 65 countries [16]. The pooled prevalence of primary clarithromycin resistance was >15% in European, Eastern Mediterranean and Western regions but were lower in the Americas (10 %, 95% CI 4-16) and the South-East Asia region (10%, 95% CI 5-16). Resistance to clarithromycin was significantly associated with failure of H. pylori eradication with a clarithromycin-containing regimen (odds ratio, 6.97; 95% CI, 5.2-9.3). However, the study was limited by significant heterogeneity and 10 of the 13 studies contributing to the pooled data for the Americas region were derived from South America. Local surveillance data are needed guide the choice of eradication regimens.

The increasing prevalence of levofloxacin resistance is one of the reasons why levofloxacin-based therapy is not advised as a first-line treatment modality for H. pylori infection. Levofloxacin should not be used for treatment unless the H. pylori strain is known to be sensitive to it or if the population's levofloxacin resistance rates are known to be less than 15% [6,16-18], particularly in nations with high quinolone consumption.

The prevalence of antimicrobial resistance in Kosovo is two to five times higher for the majority of bacteria and corresponding antibiotic groups compared with the means in EU countries [19].

For the majority of bacteria and related antibiotic families, the prevalence of antimicrobial resistance in Kosovo is two to five times greater than the average in EU nations [19].

Our study was successful in providing clear answers. To our knowledge, no other study comparing first-line levofloxacin-based therapy to first-line standard therapy, that has been published in Kosovo, in the English language.

In the future, the research for resistance of H. pylori in antimicrobial therapy, until it is necessary to select the appropriate schemes for the eradication and success of this microbe eradication.

Conclusion

In conclusion, this 10-day triple therapy combining PPI with high-dose amoxicillin and Levofloxacin two times a day is approximately well tolerated and seems effective in eradicating H. pylori as standard triple therapy in the first line.

Patient Consent Form: For all participants were obtained consent form treatment.

Scientific Responsibility Statement: The authors declare that they are responsible for the articles scientific include study design, data collection, analysis and interpretation, writing, preparation and scientific review of the contents, and approval of the final version of the article.

Author's Contribution: Zaim Gashi made a substantial contribution to the conception and design of the work. Fadil Sherifi made a substantial contribution to data analysis, preparation of the draft, and final revision of the manuscript. Arjeta Gashi made contribution in field of comparison of medical treatment and support in comparison of different treatment. All authors agree the manuscript.

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References

1. NIH Consensus Conference. (1994) Helicobacter pylori in peptic ulcer disease. NIH Consensus Development Panel on Helicobacter pylori in Peptic Ulcer Disease. JAMA 272:65.
2. Malfertheiner P, Megraud F, O'Morain CA, Atherton J, Axon ATR, et al. (2012) Management of Helicobacter pylori infection--the Maastricht IV/ Florence Consensus Report. Gut, 61:646.
3. Chey WD, Wong BC, Practice Parameters Committee of the American College of Gastroenterology. (2007) American College of Gastroenterology guideline on the management of Helicobacter pylori infection. Am J Gastroenterol 102:1808.
4. Laine L. (1993) Helicobacter pylori, gastric ulcer, and agents noxious to the gastric mucosa. Gastroenterol Clin North Am, 22:117.
5. Schistosomes, liver flukes and Helicobacter pylori. (1994) IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Lyon, 7-14 June 1994. IARC Monogr Eval Carcinog Risks Hum, 61:1.
6. Chey WD, Leontiadis GI, Howden CW, Moss SF. (2017) ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol 112:212.
7. Fallone CA, Chiba N, van Zanten SV, Fischbach L, Gisbert JP, et al. (2016) The Toronto Consensus for the Treatment of Helicobacter pylori Infection in Adults. Gastroenterology151:51.
8. Yuan Y, Ford AC, Khan KJ, Gisbert JP, Forman D, et al. (2013) Optimum duration of regimens for Helicobacter pylori eradication. Cochrane Database Syst Rev, 11:CD008337.
9. Fock KM, Katelaris P, Sugano K, Ang TL, Hunt R, et al (2009) Second Asia-Pacific Conference. Second Asia-Pacific Consensus Guidelines for Helicobacter pylori infection. J Gastroenterol Hepatol. 24:1587-600.
10. Hu Y, Zhu Y, Lu NH. (2017) Primary Antibiotic Resistance of Helicobacter pylori in China. Dig Dis Sci. 62:1146–1154.

11. Li BZ, Threapleton DE, Wang JY, Xu JM, Yuan JQ, et al. (2015) Comparative effectiveness and tolerance of treatments for Helicobacter pylori: systematic review and network meta-analysis. BMJ. 351:h4052.

12. Vakil N. (2005) Primary and secondary treatment for Helicobacter pylori in the United States. Rev Gastroenterol Disord. 5:67.

13. Kuo CH, Kuo FC, Hu HM, Liu CJ, Wang SS, et al. (2012) The optimal first-line therapy of Helicobacter pylori infection in year 2012. Gastroenterol Res Pract. 2012: 168361.

14. Malfertheiner P, Megraud F, O'Morain C, Bazzoli F, El-Omar E, et al. (2007) Current concepts in the management of Helicobacter pylori infection: the Maastricht III Consensus Report. Gut. 56: 772-81.

15. Latif S, Akther N, Amjed S, Jafar J, Saleem B, et al. (2018) Efficacy of standard triple therapy versus Levofloxacin based alternate therapy against Helicobacter pylori infection. JPMA. The Journal of the Pakistan Medical Association. 68:1295-1299.

16. Savoldi A, Carrara E, Graham DY, Conti M, Tacconelli E (2018) Prevalence of Antibiotic Resistance in Helicobacter pylori: A Systematic Review and Meta-analysis in World Health Organization Regions. Gastroenterology. 155:1372.

17. Jones NL, Koletzko S, Goodman K, Bontems P, Cadranel S, et al. (2017) Joint ESPGHAN/NASPGHAN Guidelines for the Management of Helicobacter pylori in Children and Adolescents (Update 2016). J Pediatr Gastroenterol Nutr 64:991.

18. Shah SC, Iyer PG, Moss SF. (2021) AGA Clinical Practice Update on the Management of Refractory Helicobacter pylori Infection: Expert Review. Gastroenterology 160:1831.

19. Raka L, Kurti A, Jakupi A, Krasniqi S, Turjaka A (2019) Kosovo's National Action Plan for antimicrobial resistance, Lancet Infect Dis, 19; 244.