



Comparison of Levofloxacin Versus Clarithromycin Based Triple Therapy in the Eradication of *H. Pylori* Infection in Patients Visiting Tertiary Care Hospital in Peshawar

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ABSTRACT

Background: *Helicobacter pylori* infection is a major cause of chronic gastritis, peptic ulcer disease, and gastric malignancy worldwide. The effectiveness of standard clarithromycin-based triple therapy has declined over recent years due to increasing antibiotic resistance, particularly in developing countries. Levofloxacin-based triple therapy has emerged as a potential alternative with improved eradication rates.

Objective: To compare the efficacy, safety, and compliance of levofloxacin-based versus clarithromycin-based triple therapy in eradication of *H. pylori* infection among patients attending a tertiary care hospital in Peshawar.

Methods: This comparative cross sectional study was conducted on 240 *H. pylori*-infected patients. Patients were divided into two equal groups receiving either levofloxacin-based or clarithromycin-based triple therapy for 14 days. Assessment of eradication was conducted 4-6 weeks after treatment was administered in terms of urea breath test or stool antigen test.

Results: The eradication rate was much more in levofloxacin group (85.8%) than in clarithromycin group (71.7%) ($p = 0.004$). Side effects were mild in both groups and metallic taste disturbance was significantly more common in clarithromycin group. In both groups the compliance was high.

Conclusion: Levofloxacin-based triple therapy provided higher eradication rates and comparable safety and compliance, showing it may be a more suitable first-line treatment option in regions with high clarithromycin resistance.

Introduction

Helicobacter pylori is a gram negative, spiral shaped, microaerophilic bacterium, which colonized the gastric mucosa and causes chronic inflammation that may last several decades unless treated. The organism has now become well established as a significant cause of the range of upper gastrointestinal disease conditions, including chronic active gastritis, peptic ulcer disease, and gastric malignancy. In clinical practice, this carcinogenicity is not a theoretical construct but a significant societal health issue since elimination of *H. pylori* can halt inflammation atrophy metaplasia dysplasia cascade and decrease the burden of disease over time [1].

H. pylori is one of the most prevalent chronic infections globally and its epidemiology is being disproportionately affected by low and middle income countries in which overcrowding, lack of sanitation and inadequate access to diagnostic and eradication therapy encourages early acquisition and sustained infection [2]. On top of structural determinants, *H. pylori* epidemiology is being increasingly influenced by clinical expression of infection, which is determined by bacterial virulence factors, host genetics, environmental exposures and diet, all of which combine to shape the risk of development of ulcer disease [3].

H. pylori infection is one of the most critical public health problems in Pakistan and is often diagnosed in patients presenting with dyspepsia, pains in the epigastric area, and other upper GI symptoms. The relevance of routine testing and effective eradication therapy within clinical pathways is supported by high levels of positivity among populations of symptoms under local tertiary care, and the long term goal of eradication should be to achieve high levels of eradication in the population [4].

Clarithromycin based triple therapy, which is a combination of a proton pump inhibitor, clarithromycin, and amoxicillin, has been considered an initial treatment in many years. But its performance has dropped in

the world especially as there has been an increase in clarithromycin resistance. The Maastricht VI Florence agreement notes that clarithromycin based triple therapy should not be used empirically in case of a high or unknown prevalence of clarithromycin resistance and alternative regimens should be used, which represents the reality that clarithromycin resistance greatly impairs the ability to cure [5].

H. pylori antimicrobial resistance is currently considered an international issue with significant implications on the achievement of eradication and antibiotic stewardship. Resistance to first line drugs like clarithromycin and fluoroquinolones has been proven to be much higher than guideline levels in various countries, thus limiting choices in empiric treatment, thus demonstrating the necessity of region specific regimen selection [6].

In Pakistan, the local local isolates have been characterized by molecular and clinical investigations to show alarming clarithromycin resistance and the associated mutations, and this plausibly leads to failure in treatment once clarithromycin based regimens have been utilized without the test of susceptibility. A third-generation fluoroquinolone Levofloxacin has good pharmacokinetics, tissue penetration and has proven active in the case of *H. pylori* [7,8]. Comparative clinical studies have found higher eradication rates with levofloxacin based regimens than clarithromycin based regimens in select locations supporting the potential utility of the evaluation of levofloxacin as an alternative option [9,10]. Although these developments occur, the choice of therapy should be informed by the local effectiveness and tolerability as the resistance pattern and patient factors vary between regions. Khyber Pakhtunkhwa has paucity of published comparative data of levofloxacin based on clarithromycin based triple therapy outcomes in real world tertiary care populations. Hence, the rationale of this study was to compare the efficacy, safety and patient compliance of levofloxacin based versus clarithromycin

based triple therapy in patients presenting with *H. pylori* infection to a tertiary care hospital in Peshawar to produce locally relevant evidence to enhance the first line eradication choices.

Methodology

This is a cross-sectional comparative study that was carried out in a tertiary care hospital in Peshawar, during a twelve month time frame from January 2024 to December 2024. The sample size of 240 adult patients aged between 18 and 70 years with proven *Helicobacter pylori* infection was used through non-probability consecutive sampling. The infection of *H. pylori* was diagnosed by using urea breath test, stool antigen test, a rapid urease test, or histopathological analysis of the gastric biopsy.

Patients who had been previously treated with *H. pylori* eradication treatment, patients who had been taking antibiotics within the past four weeks, and patients who were known to be hypersensitive to levofloxacin, clarithromycin or amoxicillin were excluded. The study also excluded pregnant and lactating women, patients with severe systemic illnesses, e.g. chronic liver or renal disease.

Patients were grouped into two groups at the end of the enrollment depending on the treatment regimen taught by the treating physician. One of the groups was given levofloxacin-based triple therapy composed of levofloxacin 500 mg twice in a day, amoxicillin 1 g twice in a day, and a proton pump inhibitor twice in a day over a period of fourteen days. The second group was treated with clarithromycin triple therapy of

clarithromycin 500mg twice a day, amoxicillin 1g twice a day, and a proton pump inhibitor twice a day. At the start of treatment, patients were provided with information about the importance of taking medications and possible side effects.

The follow-up of the patients occurred four to six weeks after therapy. The *H. pylori* extermination was determined by urea breath test or stool antigen test with the requirement that proton pump inhibitors should be stopped at least two weeks before the test. The side effects were reported according to the patient self-report, and the adherence was measured in terms of the pill counts and patient interviews.

Data were entered and analyzed using the **Statistical Package for the Social Sciences (SPSS)**. Continuous variables were used to display mean standard deviation whereas categorical variables were used to show the frequency and percentage. Chi-square test was used to test the eradication rates, adverse effects and compliance to treatment between the two groups. The p-value of below 0.05 was decided to be a statistically significant value.

Results

The final analysis involved 240 patients with 120 patients in the each treatment groups. The baseline demographic and clinical factors of the patients were not much different among the two groups and no statistical significant differences were found regarding age, gender distribution, body mass index, smoking status, or incidence of diabetes mellitus (Table 1).

Table 1: Baseline Demographic Characteristics

Variable	Levofloxacin Group (n=120)	Clarithromycin Group (n=120)	p-value
Mean Age (years ± SD)	44.2 ± 11.8	47.6 ± 12.9	0.18
Male	68 (56.7%)	70 (58.3%)	0.79
Female	52 (43.3%)	50 (41.7%)	
Mean BMI (kg/m ²)	25.9 ± 3.9	27.3 ± 4.1	0.06
Smokers	38 (31.7%)	41 (34.2%)	0.65
Diabetics	26 (21.7%)	29 (24.2%)	0.62

The most typical presenting symptoms in both groups were epigastric pain and dyspepsia. Clinical symptoms were equally spread, which suggested that the disease was of equal severity at the baseline (Table 2).

Table.2. Clinical Presentation of Patients

Symptom	Levofloxacin (n=120)	Clarithromycin (n=120)
Epigastric pain	92 (76.7%)	95 (79.2%)
Dyspepsia	88 (73.3%)	90 (75.0%)
Nausea/Vomiting	41 (34.2%)	44 (36.7%)
Heartburn	57 (47.5%)	61 (50.8%)
Loss of appetite	29 (24.2%)	33 (27.5%)

The urea breath test was the most frequently used diagnostic modality, followed by stool antigen testing, with no significant difference in diagnostic approaches between groups (figure 1).

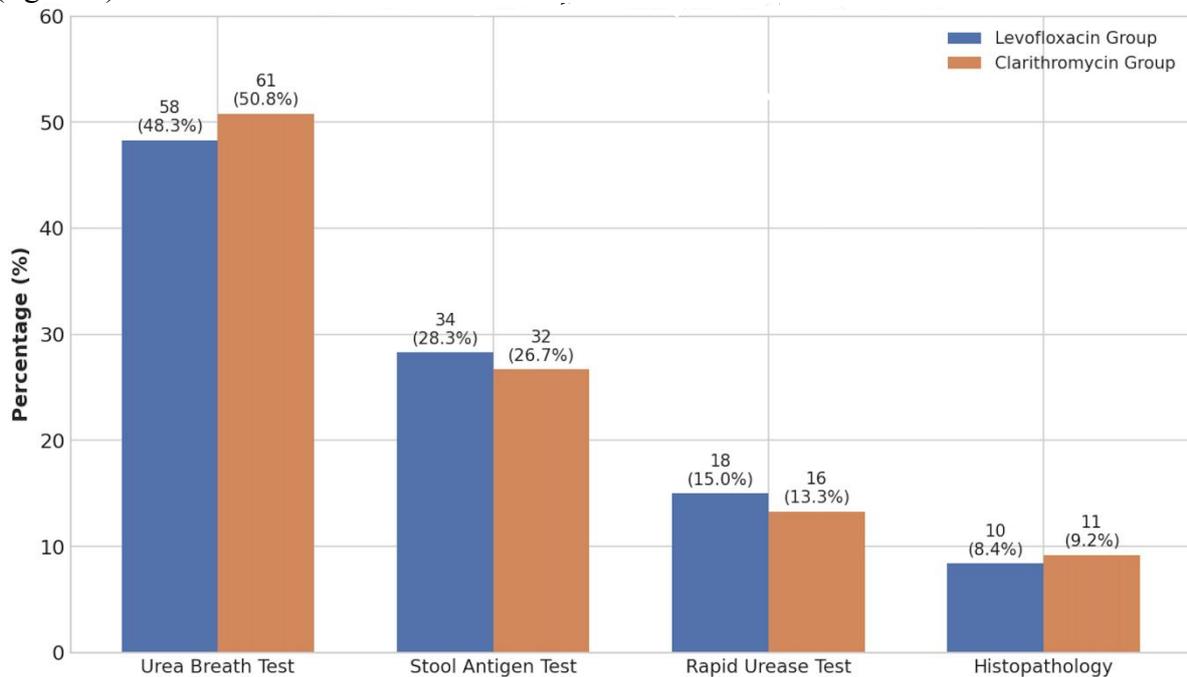


Figure.1. Distribution of diagnostic methods used for the detection of *Helicobacter pylori* infection in levofloxacin and clarithromycin treatment groups. Urea breath test was the most common used diagnostic modality in both groups followed by stool antigen testing.

H. pylori was eliminated in 103/120 patients (85.8%), who took levofloxacin-based triple therapy, and 86/120 patients (71.7%), who took clarithromycin-based triple therapy. The eradication rate disparity was also statistically significant ($p = 0.004$) indicating better effect of levofloxacin-based therapy (Figure 2).

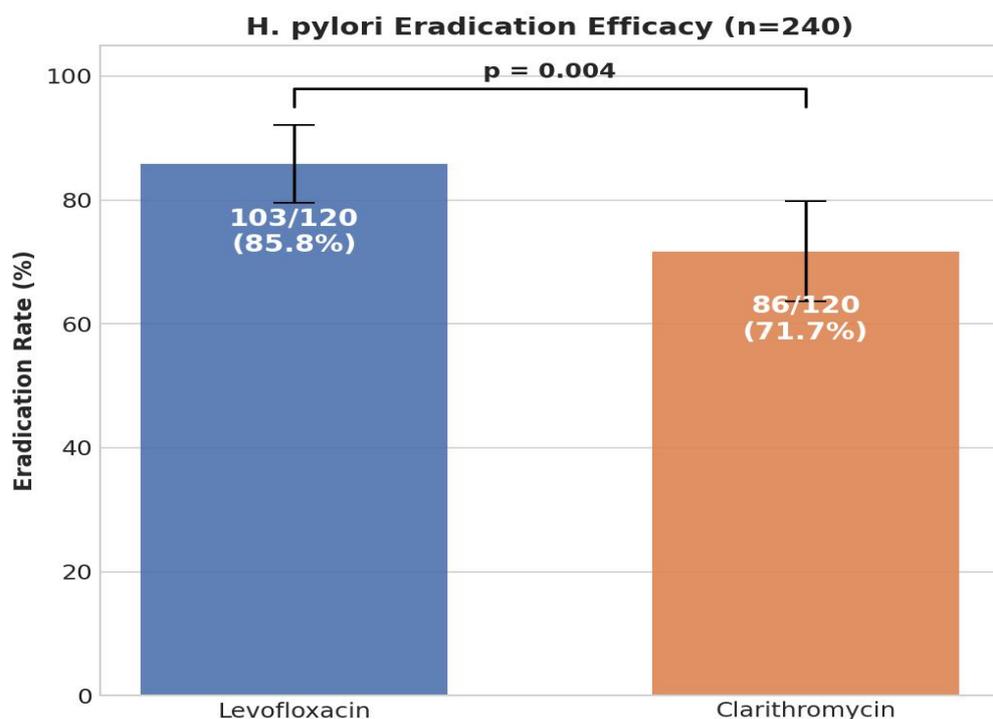


Figure 2. Comparison of the eradication rates of *H. pylori* for Levofloxacin-containing vs. Clarithromycin-containing triple therapies. Levofloxacin had a significantly higher eradication rate of 85.8% vs. 71.7% with Clarithromycin ($p = 0.004$).

The two treatment regimens were usually well tolerated. The side effects were mild and self limiting. The both groups reported nausea, headache, and diarrhea, but the metallic taste disturbance was much higher in the clarithromycin group (Table 3). No severe adverse events or accounts of hospitalization due to treatment.

Table 3: Eradication Rates by Gender

Gender	Levofloxacin Group (%)	Clarithromycin Group (%)
Male	83.3%	70.6%
Female	86.5%	73.5%

In both groups, the treatment compliance was high. There were 90.8% and 87.5% completion rates of the whole course of therapy in the levofloxacin group and clarithromycin group respectively. The clarithromycin group exhibited a slight difference in early discontinuations but it was not significant (Table 4).

Table 4: Treatment Compliance

Compliance Level	Levofloxacin Group	Clarithromycin Group
Completed full course	109 (90.8%)	105 (87.5%)
Missed ≤ 2 doses	8 (6.7%)	9 (7.5%)
Discontinued early	3 (2.5%)	6 (5.0%)

Discussion

The current research shows that triple therapy with levofloxacin was associated with a much more impressive eradication rate (85.8%) than clarithromycin-based triple therapy (71.7%) against *Helicobacter pylori* infection. This was statistically and

clinically significant because rates of over 80 eradication are usually acceptable in first-line therapy. The inability of clarithromycin-based therapy to attain this threshold is an indication of its decreased efficacy in this group.

These are compatible with the emerging international and regional data of decreased efficacy of clarithromycin-based regimens owing to increasing macrolide resistance. A number of studies have reported clarithromycin resistance to go beyond 15-20% and at this point, the standard triple therapy is no more empirically employed [11,12]. The American College of Gastroenterology and the World Gastroenterology Organisation guidelines recommend against the use of triple therapy based on clarithromycin in areas whose resistance patterns are unknown or high [13,14].

On the contrary, levofloxacin-based regimens have presented encouraging eradication rates in several comparative trials. A study shows that the therapy based on levofloxacin achieved much higher eradication rates in comparison with those of clarithromycin-based therapy (74.5% vs 62) [15]. On the same note, South Asian studies in the region have shown levofloxacin-containing regimens to eradicate 80-88% of the cases, which is very close to the present study [16,17]. These findings indicate that levofloxacin can continue to be used as an alternative in a population with a high-incidence of clarithromycin resistance.

It has also been reported that clarithromycin-based therapy is becoming less successful in Pakistan and eradication rates are dropping frequently below acceptable levels [18]. Another study identified better effects using levofloxacin-based triple therapy than the traditional clarithromycin-based therapy and suggested to reevaluate the first-line treatment approach in Pakistan [19]. We also confirm this recommendation in our findings, especially since in tertiary care the clinical implications of the failure to treat an individual are more severe.

The superior rate of eradication that was found with the levofloxacin-based therapy in this study can be partially explained by the increased compliance and tolerability of the therapy. Even though both regimens

were overall well tolerated, the occurrence of metallic taste disturbance significantly increased in the clarithromycin arm, which is a side effect that has been well-documented in the past and has been identified to have a negative effect on adherence [20]. Although the overall adherence was the same in both groups, the population of the levofloxacin group was slightly higher, which might have resulted in better results.

There was no significant difference in gender based eradication rates in groups, meaning that sex was not a significant factor in treatment response. This finding is in line with previous reports who established that there is no significant correlation of gender and H. pylori eradication success in situations where the level of adherence is satisfactory [21].

Regardless of its merits, this research has weaknesses. The single-center design can be a limitation in the generalization of the study to other areas. Also, antibiotic susceptibility testing was not conducted and it could not be directly correlated to failure of eradication and resistance patterns. The existing recommendations pay a growing focus to the susceptibility-guided therapy, which will maximize the outcomes and decrease antimicrobial resistance [13,22]. It is also important to note that the latest and gold standard therapy for eradication of H Pylori infection is Bismuth Quadruple Therapy and it's far superior than any of these standard Clarithromycin or Levofloxacin based tripple therapies.

To sum up, this research indicates that triple therapy based on levofloxacin would be more effective and acceptable than clarithromycin-based triple therapy in eradicating H. pylori in this group of people. Since the clarithromycin resistance rate is on the increase in Pakistan, the change in the empirical approach to treatment and the use of alternative regimens or susceptibility-directed therapy needs to be highly regarded.

Conclusion:

Triple therapy using levofloxacin showed more eradication rates than the use of

clarithromycin-based therapy, and similar safety, toleration, and adherence were observed. These results indicate that a levofloxacin-based treatment can be associated with better treatment effectiveness and a low probability of side-effects. Levofloxacin-based triple therapy seems to be a better option of the first-line therapy in the treatment of *Helicobacter pylori* infection in regions where resistance to clarithromycin is widespread. Integrating the patterns of local antibiotic resistance into the choice of treatment could result in greater eradication rates and lower chances of treatment failure and disease recurrence.

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