



# A Systematic Review On Efficacy Of Bismuth-Based Triple Vs. Standard Triple Therapy For Eradication Of Helicobacter Pylori

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## ABSTRACT

**IMPORTANCE:** Helicobacter pylori (H. pylori) infection is a common global health concern linked to chronic gastritis, peptic ulcers, and gastric cancer. Eradication regimens have evolved over the decades due to growing antibiotic resistance. While the standard triple therapy has long been the first-line treatment, its efficacy has diminished in many regions. Bismuth-based therapies, including triple and quadruple combinations, have gained attention due to their broader activity against resistant strains. Its implementation could significantly improve treatment outcomes, reduce recurrence, and serve as a more effective first-line strategy in regions with high antibiotic resistance. **OBJECTIVE:** The objective of the article is to systematically review and compare the efficacy of Bismuth-Based Triple Therapy vs. Standard Triple Therapy for Eradication of Helicobacter pylori. **METHODS:** A thorough search of the literature was done for research published between 2000 and 2024 using PubMed, Scopus, and the Cochrane Library. We considered prospective, observational, and randomized controlled trials that compared BT with ST in patients with H. pylori infection who had not received therapy. The results of safety, antibiotic resistance profiles, and eradication rates (both intention-to-treat and per-protocol) were significant. **CONCLUSION:** In terms of eradication success, bismuth-based triple therapy is superior than normal triple therapy and had to be chosen, particularly in areas with significant resistance. Adding vonoprazan or customized regimens increases efficacy. Future recommendations had to support first-line treatments tailored to a given location and take resistance trends into account.

**KEYWORDS:** Bismuth based, GI Infection, Resistance, H. pylori, vonoprazan.

## INTRODUCTION

Helicobacter pylori is a Gram-negative microaerophilic spiral bacterium which colonizes gastric mucosa and is involved in the pathogenesis of peptic ulcer disease, gastric adenocarcinoma, and MALT lymphoma. H. pylori has been perceived as an important worldwide public health concern since its discovery in 1982 by Barry Marshall and Robin Warren [1]; it is believed that 50% of the planet's population is infected [2]. Its prevalence is particularly high in underdeveloped nations largely due to poor sanitation, crowded living conditions, and restricted healthcare services.

Infection with H. pylori has significant clinical consequences. The bacterium causes persistent inflammation, which can result in consequences like cancer or bleeding ulcers, in addition to gastrointestinal symptoms like bloating, dyspepsia, and stomach pain. Effective H. pylori removal is therefore crucial for both symptom relief and the long-term prevention of severe gastrointestinal disorders.

For more than 20 years, the first-line treatment of *H. pylori* infection has been based on the standard triple therapy (STT), including a proton pump inhibitor (PPI) and two antibiotics, e.g., clarithromycin and either amoxicillin or metronidazole. But STT has the limitation that it is highly dependent on antibiotic susceptibility. STT has been challenged worldwide by escalating resistance to clarithromycin and metronidazole, with eradication rates of less than 70% reported in several areas, predominantly in Asian, African, and Southern European countries. This indicates an apprehensive demand for alternate regimens which may respond effectively to antibiotic resistance.

In recent years, a large number of observational cohorts, meta-analyses, and randomized controlled trials (RCTs) have been published comparing the effectiveness of BTT with STT. There is a wide range of results from these studies since they differ in terms of location, length of time, antibiotic combinations, and diagnostic techniques (such as stool antigen, histology, and urea breath test). However, there is a persistent pattern of BTT being more effective than STT, or at least as effective, especially in situations when clarithromycin resistance is present. Furthermore, adding bismuth seems to work in concert with antibiotics to improve bacterial eradication and overcome partial resistance.

Bismuth-based therapies, initially developed as quadruple regimens involving bismuth, metronidazole, tetracycline, and a PPI, have resurfaced as viable first-line treatments due to their ability to bypass clarithromycin resistance. By interfering with the bacterial cell wall and biofilm development, bismuth compounds have direct antibacterial activity [3] and work in concert with antibiotics to increase their effectiveness. Building on this, bismuth-based triple therapy (BBTT) has become popular as a streamlined regimen with strong efficacy, particularly for patients who have never received treatment before or who reside in areas where antibiotic resistance is known.

The field of *H. pylori* eradication has advanced even more recently with the development of vonoprazan, a potassium-competitive acid blocker (P-CAB). Vonoprazan suppresses stomach acid more quickly, powerfully, and persistently than PPIs, which is essential for optimizing antibiotic stability and efficacy. Even in resistant strains, its usage in conjunction with antibiotics and bismuth (BBTT or even quadruple regimens) has produced encouraging results.

East Asian clinical trials, especially those in China and Japan, have shown that vonoprazan-based treatments are superior to traditional PPI-based STT. For example, a 14-day vonoprazan-bismuth triple therapy outperformed both STT and bismuth quadruple therapy (BQT), achieving eradication rates in treatment-naïve patients that exceeded 90% [1]. Similar to this, VQ HP study in Thailand in 2023 revealed encouraging outcomes for vonoprazan-bismuth regimens in areas with high levels of levofloxacin and clarithromycin resistance [2].

When choosing a therapy, patient compliance and side effects are important factors in addition to resistance problems. Treatment success may be decreased by regimens that result in poor adherence due to gastrointestinal discomfort or a high pill burden. When correctly developed, BTT regimens have the potential to be more effective than BQT over shorter periods of time and with fewer adverse effects.

This systematic review compares the effectiveness, safety, and tolerability of BBTT with STT in the eradication of *H. pylori*, with an emphasis on treatment-naïve individuals, in light of changing resistance patterns and therapeutic developments. This study aims to support evidence-based updates to treatment guidelines and assist clinical decision-making by combining data from real-world research, randomized controlled trials, and international experiences.

## METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [5] guidelines were followed in the conduct of this systematic review. The goal was to evaluate the safety and effectiveness of conventional triple therapy (STT) and bismuth-based triple therapy (BBTT) in eliminating *Helicobacter pylori* in patients who had never received treatment.

### Search Strategy:

The study employed a thorough literature search strategy that covered the period from January 2015 to April 2025 in three electronic databases: PubMed, Scopus, and Google Scholar. The keywords utilized were: "Helicobacter pylori", "bismuth-based triple therapy", "standard triple therapy", "vonoprazan", "clarithromycin resistance", "treatment-naive", along with "eradication rate". To combine phrases, Boolean operators (And, Or) were employed. By manually screening the references of important articles, more sources were found.

### Inclusion Criteria:

- Research design: prospective cohort studies, well-conducted observational studies, or randomized controlled trials (RCTs).
- Population: Patients with a confirmed *H. pylori* infection who have not received treatment.
- Intervention: Triple therapy based on bismuth, either with or without vonoprazan.
- Comparator: PPI + clarithromycin + amoxicillin/metronidazole (Standard triple therapy).
- Outcomes: Primary outcomes included *H. pylori* eradication rates (intention-to-treat [ITT] and per-protocol [PP]). Secondary outcomes included adverse effects and dropout rates.
- Language: Articles published in English.

### Exclusion Criteria:

- Research that does not directly compare STT and BBTT.
- Research that only examined quadruple therapy, excluding BBTT.
- Editorials, Case studies, Research articles, Reviews, or research on animals.
- Research on second-line therapy or salvage therapy.

### Data Extraction and Management:

Eligibility was assessed by two independent reviewers who looked at entire texts, abstracts, and titles. A third reviewer or conversation were used to settle disagreements. Relevant data was extracted using a standardized data collecting form, which included:

- Features of the study (author, year, nation, design, sample size)
- Patient characteristics;
- Treatment plans (dosage, duration, and combinations of drugs);
- ITT and PP eradication rates;
- Adverse events and tolerability;
- Resistance trends and local data

### Quality Assessment:

The Cochrane Risk of Bias (RoB 2.0) [6] tool was used to evaluate RCTs, assessing areas like blinding, allocation concealment, randomization, and outcome reporting. The Newcastle-Ottawa Scale (NOS) [7] was used to evaluate observational studies, with an emphasis on outcome evaluation, comparability, and selection. High quality studies were defined as having a NOS score of  $\geq 7$  or a low risk of bias in RoB 2.0.

### Data Synthesis:

A qualitative synthesis was given priority because study designs and outcome measures varied widely. When available, eradication rates were presented as percentages with matching confidence intervals. Subgroup analysis was used whenever feasible to investigate the effects of vonoprazan inclusion, treatment duration, antibiotic resistance, and regional prevalence.

## RESULTS

### Eradication Rates

The eradication rate for BBTT was 88.7% (ITT) in the multicentre RCT versus 72.5% for STT, with a statistically significant difference ( $p<0.01$ ) [4]. In a Belgian cohort, showed similar results, with BBTT achieving 90.2% eradication compared to 67.3% for STT [8].

A 14-day vonoprazan-based bismuth quadruple treatment outperformed STT in the VQ HP trial especially in areas with high levels of clarithromycin resistance ( $>30\%$ ). This lends credence to the idea that the profile of antibiotic resistance and the degree of acid suppression are important factors [2].

### Antibiotic Resistance and Regional Variations

The effectiveness of STT has been significantly hampered by resistance to levofloxacin and clarithromycin, particularly in Asia and Africa. According to the Democratic Republic of the Congo has STT failure rates of above 40%. On the other hand, BBTT, which combines metronidazole with either furazolidone or tetracycline, maintained its great effectiveness in spite of resistance [4].

### Safety and Tolerability

Both regimens were generally well tolerated throughout investigations. Minor gastrointestinal adverse effects, including as nausea and darker stools from bismuth, were more common in BBTT. Nonetheless, the groups' dropout rates from negative consequences were similar ( $<5\%$ ) [9].

### Paediatric and Special Populations

In their study of children with *H. pylori* infection, discovered that BBTT was more effective (86.4% vs. 64.3%) and had good tolerability [7]. This is consistent with research that pointed out that BBTT might work well as a first-line treatment for patients of all ages [5].

### Vonoprazan-Based Regimens

Numerous studies demonstrated that using vonoprazan in place of a traditional proton pump inhibitor increased the effectiveness of BBTT. Real-world data shown that vonoprazan-based BBTT produced eradication rates above 90%, even in patients who had experienced dual resistance or previous treatment failure. The notion that greater acid suppression enhances antibiotic action and eradication results is supported by this [9].

## CONCLUSION

In conclusion, there is substantial evidence that BBTT is a more successful and equally tolerated first-line regimen than STT. This is especially important in areas where empirical treatment decisions must be made and antibiotic susceptibility testing is not regularly available. Incorporating BBTT, particularly vonoprazan-enhanced regimens, into standard clinical practice for *H. pylori* eradication should be taken into consideration by national and international recommendations. To maximize eradication methods in the age of rising antibiotic resistance, future research should give priority to cost-effectiveness analysis, head-to-head comparisons across different demographic groups, and the creation of region-specific treatment algorithms.

## ACKNOWLEDGEMENT

We thank the management, doctors, and nursing staff of the Department of Pulmonology, PK Das Institute of Medical Sciences, Kerala.

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