Advantages of Moxifloxacin and Levofloxacin-based triple therapy for second-line treatments of persistent Helicobacter pylori infection: a meta analysis

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Vorteile einer Moxifloxazin beziehungsweise Laevofloxaazin basierten Triple Therapie als Second-line Behandlung einer persistenten Infektion mit Helicobacter pylori: Eine Metaanalyse


Ergebnisse: Die berichteten Eradikationsraten zeigten, dass die Clarithromycin basierte Triple Therapie der Bismuth basierten Quadrupel Therapie unterlegen zu sein scheint (OR = 0,53; 95 % CI: 0,35–0,80; P = 0,002). 13 RCTs verglichen eine Laevofloxaazin basierte Triple Therapie mit einer Bismuth basierten Quadrupel Therapie – diese 2 Therapiearten unterschieden sich bezüglich ihres Eradikationserfolges nicht signifikant (OR = 1,43; 95 % CI: 0,82–2,51; P = 0,21). Allerdings waren die Eradikationsraten der 10-tägigen Laevofloxaazin basierte Triple Therapie einer 7tägigen Bismuth basierten Quadrupel Therapie signifikant überlegen (OR = 4,79; 95 % CI: 2,95–7,79; P < 0,00001). Die Laevofloxaazin basierte Triple Therapie wurde besser vertragen als die Bismuth basierte Quadrupel Therapie (OR = 0,41; 95 % CI: 0,27–0,61; P < 0,0001) und musste auch seltener wegen Nebenwirkungen abgebrochen werden (OR = 0,13; 95 % CI: 0,06–0,33; P < 0,0001). Außerdem lässt das Ergebnis unserer Meta Analyse vermuten, dass die Eradikationsraten der Moxifloxaazin-basierten Tripel Therapie der Bismuth basierten Quadrupel Therapie geringfügig – allerdings ohne statistische Signifikanz – überlegen ist.


Summary. Objective: The main aim of this meta-analysis was to compare the efficacy and safety of clarithromycin and second-generation fluoroquinolone-based triple therapy vs. bismuth-based quadruple therapy for the treatment of persistent Helicobacter pylori infection.

Methods: A systematic literature search was conducted for articles and abstracts from 1981 to March 2009 using Medline, PubMed, EMBase, Google Scholar and CNKI (Chinese), Wanfang (Chinese) digital database and recent Digestive Disease Week, United European Gastroenterology Week, and European Helicobacter Study Group conferences were also performed. Boolean operators (NOT, AND, OR) were used in succession to narrow and widen the search. Sixteen articles and four abstracts met the inclusion criteria, and were included in the meta-analysis by using Review Manager 4.2.8.

Results: The eradication rates demonstrated that clarithromycin-based triple therapy is inferior to bismuth-based quadruple therapy (OR = 0.53, 95% CI: 0.35–0.80, P = 0.002). Thirteen RCTs compared levofloxaazin-based triple therapy vs. bismuth-based quadruple therapy, the
eradication rates of the two regimens were shown to have no significant difference (OR = 1.43, 95% CI: 0.82–2.51, P=0.21). But the eradication rates demonstrated superiority of the 10-day levofloxacin-based triple therapy over 7-day bismuth-based quadruple therapy (OR = 4.79, 95% CI: 2.95–7.79, P<0.00001). Levofloxacin-based triple therapy was better tolerated than bismuth-based quadruple therapy with lower rates of side effects (OR = 0.41, 95% CI: 0.27–0.61, P<0.00001), and lower rates of discontinuation of therapy due to adverse events (OR = 0.13, 95% CI: 0.06–0.33, P<0.00001). Furthermore, our meta-analysis suggested that the eradication rates of the moxifloxacin-based triple therapy has a slight superiority to bismuth-based quadruple therapy, but there was no significant difference between them.

**Conclusion:** Second-generation fluoroquinolone-based triple therapy can be suggested as the regimen of choice for rescue therapy in the eradication of persistent *H. pylori* infection especially 10-day levofloxacin-based triple therapy.

**Key words:** PPI, bismuth, levofloxacin, moxifloxacin, fluoroquinolone, *Helicobacter*, eradication rate, second-line treatment.

**Introduction**

*Helicobacter pylori* infection plays an important role in the pathogenesis of chronic gastritis, peptic ulcer disease, gastric mucosa-associated lymphoid tissue lymphoma, and gastric malignancies [1–4]. Recently, several studies have suggested that *H. pylori* is also involved in the development of coronary heart disease [5], idiopathic thrombocytic purpura [6] and gastroesophageal reflux disease [7]. *H. pylori* is a major cause of illness and death worldwide [4]; therefore, eradication of *H. pylori* has become an important consideration in the treatment of these diseases. This is especially true regarding the natural history of both peptic ulcer disease and gastric lymphoma [8]. Many worldwide consensus conferences have recommended triple therapy consisting of a proton-pump inhibitor (PPI) and two antibiotics as first-line eradication therapy [9]. But, the increasing prevalence of *H. pylori* strains resistant to antibiotics has led to increasing rates of treatment failure [10–12]. Thus, a number of second-line therapies are recommended such as: quadruple therapy [proton-pump inhibitor (PPI), bismuth, tetracycline and metronidazole] for 1 week or 2 weeks, PPI-based triple therapies for 1 week or 10 days or 2 weeks [13]. An ideal therapy should be short, have few side effects, good compliance, the low rates of bacterial resistance and high rates of eradication [14].

Although many studies have reported on the efficacy PPI-based triple therapy vs. bismuth-based quadruple therapy as second-line treatment of *H. pylori* infection, there is no consensus. Some articles have reported that bismuth-based quadruple therapy was preferred as the second-line treatment of *H. pylori* infection because this regimen had many advantages such as wide availability, low cost and reasonably good efficacy. However, other articles have shown that PPI-based triple therapies have many advantages such as fewer side effects, better compliance, lower resistance and higher eradication rates in favor of this combination as the best regimen [14]. Many articles have stated that the two therapies are equally effective as second-line treatments for *H. pylori* infection. It is also well known that in Europe, that the recommended treatment duration is usually 7 days, whereas in the United States, the Food and Drug Administration has approved regimens of 7, 10, or 14 days [9, 15]. In fact, different treatment duration may not significantly affect the results according to many studies.

Recently, a meta-analysis of levofloxacin-based triple therapy versus bismuth-based quadruple therapy for persistent *Helicobacter pylori* infection was reported by Saad et al. [14]. They showed that a 10-day course levofloxacin triple therapy was more effective and better tolerated than 7-day bismuth-based quadruple therapy in the treatment of persistent *H. pylori* infection. Moreover, another meta-analysis of levofloxacin-based rescue regimens after *Helicobacter pylori* treatment failure was reported by Gisbert JP [16]. However, since the number of subjects in two meta-analysis were not large enough, we added several proximal studies to compare levofloxacin-based triple therapy vs. bismuth-based quadruple therapy. In addition, they only compared levofloxacin-based triple therapy with bismuth-based quadruple therapy. Moxifloxacin-based and clarithromycin-based triple therapy, which are still accepted in many countries were not mentioned, and patients with drug resistance were also not shown. For this main reason, we performed a systematic literature review and meta-analysis of randomized controlled trials (RCTs) with different regimens as salvage for *Helicobacter pylori* infection. Our primary objective was to compare the efficacy of fluoroquinolone-based triple therapy and bismuth-based quadruple therapy for the treatment of persistent *Helicobacter pylori* infection. The second objective was to compare the safety of the two therapies.

**Materials and methods**

**Study sources and searches**

We searched PubMeD, MEDLINE, EMBASE, Google Scholar, CNKI (Chinese) and Wanfang (Chinese) digital database and recent Digestive Disease Week, United European Gastroenterology Week, and European Helicobacter Study Group conferences for relevant articles and articles published in English and Chinese from 1981 to March 2009. The search was limited to human studies, but was otherwise unrestricted. MeSH terms and keywords used to identify articles included “second-line treatment”; “rescue therapy”; “salvage therapy”; “*Helicobacter pylori*”, “*H. pylori*”, “proton-pump inhibitor”; “bismuth”; “levofloxacin”, “moxifloxacin”, “quinolones”, “triple therapy”, “quadruple therapy”, and “treatment”. Boolean operators (NOT, AND, OR) were used in succession to narrow and widen the search.

**Study selection**

For the meta-analysis, all studies had to meet the following inclusion criteria: (1) A study had to describe an RCT. (2) All patients had to have failed one foregoing course of *H. pylori* eradication therapy. (3) Confirmation of infection eradication at least 4 weeks after completion of treatment (based on urea breath test or gas-