

中文題目：探討幽門螺旋桿菌除菌治療對於腸道菌叢抗藥性以及抗藥性基因組之短期與長期的影響 一項多中心之隨機分派臨床試驗

英文題目：Exploring the short-term and long-term impacts of *H. pylori* eradication on the antibiotic resistance and resistome of gut microbiota-a multicenter randomized trial

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**前言 (Background):** Emergence of antibiotic resistance is an important concern for the widespread use of antibiotics. We aimed to compare the efficacy, tolerability, and long-term changes of antibiotic resistome of gut microbiota and metabolic parameters after levofloxacin-based quadruple therapy and bismuth quadruple therapy for *Helicobacter pylori* infection.

**材料及方法 (Materials and Methods):** This was a multi-center, open labeled, randomized trial. Eligible patients with *H. pylori* infection who failed after first-line eradication therapy were randomized in a 1:1 ratio to receive either levofloxacin quadruple therapy containing esomeprazole, amoxicillin, metronidazole, and levofloxacin for 14 days (**EAML**) or bismuth quadruple therapy containing esomeprazole, bismuth, tetracycline, and metronidazole for 10 days (**BQ**). The primary end point was the eradication rate in the second-line treatment according to intention-to-treat (ITT) analysis. The short-term and long-term changes of antibiotic resistome of fecal microbiota after eradication therapy determined by shotgun metagenomic sequencing were the secondary outcomes. Shotgun metagenomic libraries were generated with the Illumina DNA Prep Kit and were then sequenced on the NovaSeq 6000 Sequencing platform (2 × 150 bp). The matrix-assisted laser desorption ionization Biotyper system (Bruker, Germany) was used to identify the colonies of *K. pneumoniae* and *E. coli*, which were then submitted for sub-culture and susceptibility testing.

**結果 (Results):** We recruited 560 patients in 8 hospitals in Taiwan. The eradication rate in the second-line treatment in the EAML and BQ groups were 87.9% (246/280) and 87.5% (245/280) according to ITT analysis (p=0.898), respectively. The frequencies of any adverse effects were 48.4% (134/277) and 77.3% (211/273) in the EAML and BQ groups, respectively (p<0.0001). There was a significant increase in total and various subtypes of resistome two weeks after EAML (p=0.0074) and BQ (p=0.037) at week 2, which were restored to pretreatment level since week 8. The resistance rates to levofloxacin, ciprofloxacin, ampicillin and various cephalosporins of *Escherichia coli* and *Klebsiella pneumoniae* were significantly increased in the EAML group than in the BQ group at week 2, which were restored at week 8 and 1 year. The transient perturbation of the diversity of fecal microbiota at week 2 was also restored to basal state 1 year after levofloxacin and bismuth quadruple therapy. The prevalence of metabolic

syndrome was not altered after eradication therapy.

**結論 (Conclusion):** Levofloxacin quadruple therapy and bismuth quadruple therapy are similarly effective in the second-line treatment for *H. pylori* infection. The transient increase of antibiotic resistance/resistome and perturbation of diversity of fecal microbiota were restored to basal state 1 year after eradication therapy.

**Keywords:** refractory *H. pylori*, resistance, genotypic, susceptibility testing, third-line