Second-line levofloxacin-based quadruple therapy versus bismuth-based quadruple therapy for *Helicobacter pylori* eradication and long-term changes to the gut microbiota and antibiotic resistome: a multicentre, open-lable, randomized controlled trial

Liou, J. M, *et al*. Taiwan Gastrointestinal Disease and Helicobacter Consortium (2023).The lancet. Gastroenterology & hepatology, 8(3), 228–241.

Presenter: Hsin-Yu Wu **Date/Time:** 2024/12/12,16:10 -17:00

Commentator: Dr. Hsiu-Chi Cheng **Location:**Room 601, Med College Building

Background: *Helicobacter pylori* (*H. pylori*) infection can lead to gastric cancer; thus, it is important to eradicate *H. pylori*. On the other hand, antibiotic resistance is a global health threat that makes disease treatment more challenging. While eradication of *H. pylori* can reduce the incidence of gastric cancer, the appearance of antibiotic resistance has made the treatment for infectious diseases therapy more difficult. Levofloxacin-based sequential therapy (EAML14) and bismuth-based quadruple therapy (BQ-10) are both recommended as second-line treatments for *H. pylori* infection. However, metronidazole, which is a component of bismuth quadruple therapies, has a universe bactericide effect on gut microbes, especially anaerobic microbes. Moreover, in the last ten years, resistance to levofloxacin has significantly increased, especially in *Escherichia coli* (*E. coli*), which is a common pathogen for urinary tract infection. The gut microbiota is an important reservoir for antibiotic resistance. Whether dose bismuth-based quadruple therapy or levofloxacin-based sequential quadruple therapy change the component of gut microbiota, increase the antibiotic resistance, or metabolic parameters? Whether there are adverse effects short-term or long-term, if it does really change the gut microbiota?

Objective/Hypothesis: To investigate the component and resistome of gut microbiota among subjects before and after they received levofloxacin-based sequential quadruple therapy or bismuth-based quadruple therapy for the second-line treatment of *H pylori* infection.

Results: The 16S rRNA sequencing results show that the alpha-diversity and number of gut microbiotas had significant differences between EAML14 or BQ10 at week 2, week 8, and 1 year after treatment. BQ10 had lower alpha-diversity and number than EAML14. A recovery trend of alpha-diversity from week 2 to 1 year was noted but the trend was slower in the BQ10 group than the EAML14 group. Moreover, the abundance had a similar trend with the alpha-diversity, but the recovery was incomplete for both treatment methods.

To analyze antibiotic resistance genes (ARG), they used shotgun sequencing, results showed that the total resistome significantly increased at week 2 after treatment with EAML14 and BQ10 but returned to pre-treatment levels by week 8. Compared to the BQ10 group, the resistance of *E. coli* to levofloxacin significantly increased in the EAML14 group at week 2 but returned to pre-treatment levels by week 8 and year 1, with no significant differences between the two groups. The prevalence of metabolic syndrome did not increase in either group, or insulin resistance decreased up to one year after eradication therapy, insulin resistance was calculated according to the homoeostatic model assessment for insulin resistance.

Conclusion: Although there is a temporary increase in antibiotic resistance after eradication, these effects generally return to baseline within 2 months to 1 year. There is no increased risk of metabolic syndrome, and insulin resistance decreases after *H. pylori* eradication. The short-term rise in antibiotic resistance was reversible after *H. pylori* eradication; however, the gut microbiota disruption was incompletely reversed. The long-term effect due to gut microbiota disruption should be validated in the future.