

Clarithromycin- versus Metronidazole-Based Triple Therapy as First-Line Eradication for *Helicobacter pylori*

H. pylori is a gram-negative bacterium that colonizes human gastric mucosa and then causes a wide variety of gastric disorders. Chronic gastric infection due to *H. pylori* initially causes chronic active gastritis, which can then lead to the development of peptic ulcers, atrophic gastritis, gastric cancer, and mucosa-associated lymphoid tissue lymphoma^[1]. However, it should be noted that eradication of *H. pylori* reduces the risk for gastric cancer even in the presence of severe gastric atrophy and intestinal metaplasia^[2]. Thus, *H. pylori* eradication is the most effective strategy for prevention of gastric cancer.

Proton pump inhibitor (PPI)-containing triple therapy with amoxicillin (AMPC) and clarithromycin (CAM) is widely used as a first-line eradication therapy for *H. Pylori*^[3]. Patients who demonstrate first-line eradication treatment failure are usually treated with PPI containing triple therapy comprising AMPC and metronidazole (MNZ)^[4, 5]. Although a multicenter study conducted in 2001 reported that the eradication rate using first-line therapy was around 90%, the rate decreased to 70–80% in 2014^[4, 6]; a possible explanation for the decreased eradication rate is the prevalence of CAM-resistant *H. pylori*^[7, 8].

A prospective randomized controlled study published in 2017 aimed to compare the efficacy of CAM-based and metronidazole (MNZ)-based triple therapy in terms of *H. pylori* eradication. In this study, a total of 140 patients who underwent esophagogastroduodenoscopy for further examination and follow-up of upper gastrointestinal symptoms and *H. pylori* -associated diseases including peptic ulcers and chronic gastritis at Kindai University Hospital in Japan from June 2013 to August 2015 and Patients who underwent esophagogastroduodenoscopy for follow-up of post endoscopic submucosal dissection for early gastric cancer were enrolled^[9].

Patients were randomly divided into two groups: EAC ($n = 68$) group and EAM ($n = 72$) group. Patients in the EAC group were administered esomeprazole 20 mg, CAM 400 mg, and AMPC 750 mg twice a day for 7 days, and those in the EAM group were administered esomeprazole 20 mg, MNZ 500mg, and AMPC 750 mg twice a day for 7 days, two patients in each group dropped out owing to loss to follow-up or poor treatment compliance. Assessment of *H. pylori* infection was performed via rapid urease tests, culture methods, serum *H. pylori* antibody tests, and stool *H. pylori* antigen tests. Patients were regarded as *H. pylori* -positive when at least one of these tests yielded positive results^[9].

H. pylori eradication rates were calculated via intention- to-treat and per protocol analysis and the eradication rates in the EAC and EAM groups were calculated in patients harboring CAM-susceptible and CAM-resistant strains. This study results in: *H. pylori* eradication rates per the ITT and PP analyses were 70.6% (48/68) and 72.7% (48/66), respectively, in the EAC group. and the eradication rates were 91.7% (66/72) and 94.3% (66/70), respectively, in the EAM group. Thus, the eradication rates in the EAM group were significantly higher than those observed in the EAC group, as for the eradication rates were 87.9% (29/33) and 51.9% (14/27) in EAC-treated patients harboring CAM-susceptible and CAM-resistant *H. pylori* strains, respectively. In contrast, the eradication rates were 90.9% (40/44) and 95.7% (22/23) in EAM-treated patients bearing CAM susceptible and CAM-resistant *H. pylori* strains, respectively. None of the patients who completed the first-line eradication therapy showed serious adverse effects that required discontinuation of eradication therapy^[9].

In conclusion MNZ-based triple therapy consisting of esomeprazole and amoxicillin is superior to CAM based triple therapy containing esomeprazole and amoxicillin as first-line eradication treatment against *H. pylori* .Future studies directly comparing the efficacy and safety of *H. pylori* eradication regimens are necessary to establish an appropriate regimen as a first-line treatment.

References:

- 1- Malfertheiner P, Megraud F, O'Morain CA, Gisbert JP, Kuipers EJ, Axon AT, Bazzoli F, Gasbarrini A, Atherton J, Graham DY, Hunt R, Moayyedi P, Rokkas T, Rugge M, Selgrad M, Suerbaum S, Sugano K, El-Omar EM, European Helicobacter and Microbiota Study Group and Consensus panel: Management of *Helicobacter pylori* infection – the Maastricht V/Florence Consensus report. *Gut* 2017; 66: 6–30
- 2- Fukase K, Kato M, Kikuchi S, Inoue K, Uemura N, Okamoto S, Terao S, Amagai K, Hayashi S, Asaka M, Japan Gast Study Group: Effect of eradication of *Helicobacter pylori* on incidence of metachronous gastric carcinoma after endoscopic resection of early gastric cancer: an open-label, randomised controlled trial. *Lancet* 2008; 372: 392–397.
- 3- Nishida T, Tsujii M, Tanimura H, Tsutsui S, Tsuji S, Takeda A, Inoue A, Fukui H, Yoshio T, Kishida O, Ogawa H, Oshita M, Kobayashi I, Zushi S, Ichiba M, Uenoyama N, Yasunaga Y, Ishihara R, Yura M, Komori M, Egawa S, Iijima H, Takehara T: Comparative study of esomeprazole and lansoprazole in triple therapy for eradication of *Helicobacter pylori* in Japan. *World J Gastroenterol* 2014; 20: 4362–4369.
- 4- Nishizawa T, Maekawa T, Watanabe N, Harada N, Hosoda Y, Yoshinaga M, Yoshio T, Ohta H, Inoue S, Toyokawa T, Yamashita H, Saito H, Kuwai T, Katayama S, Masuda E, Miyabayashi H, Kimura T, Nishizawa Y, Takahashi M, Suzuki H: Clarithromycin versus metronidazole as first-line *Helicobacter pylori* eradication: a multicenter, prospective, randomized controlled study in Japan. *J Clin Gastroenterol* 2015; 49: 468–471.
- 5- O'Connor A, Gisbert JP, O'Morain C, Ladas S: Treatment of *Helicobacter pylori* infection 2015. *Helicobacter* 2015; 20(suppl 1):54–61.
- 6- Asaka M, Sugiyama T, Kato M, Satoh K, Kuwayama H, Fukuda Y, Fujioka T, Takemoto T, Kimura K, Shimoyama T, Shimizu K, Kobayashi S: A multicenter, double-blind study on triple therapy with lansoprazole, amoxicillin and clarithromycin for eradication of *Helicobacter pylori* in Japanese peptic ulcer patients. *Helicobacter* 2001; 6: 254–261.
- 7- Okamura T, Suga T, Nagaya T, Arakura N, Matsumoto T, Nakayama Y, Tanaka E: Antimicrobial resistance and characteristics of eradication therapy of *Helicobacter pylori* in Japan: a multi-generational comparison. *Helicobacter* 2014; 19: 214–220.
- 8- Hu Y, Zhang M, Lu B, Dai J: *Helicobacter pylori* and antibiotic resistance, a continuing and intractable problem. *Helicobacter* 2016; 21: 349–363.
- 9- Teppei A, Shigenaga m, Tomohiro W, Kazuki O, Ayana O, Masashi K, et al. Comparative Study of Clarithromycin- versus Metronidazole-based triple therapy as first-line eradication for *Helicobacter pylori*. *Oncology*, 2017; 93(suppl 1):15–19.

Done by pharm D: Dua'a Alrahahleh

Supervised by pharm D : Eshraq Al-Abweeny