



Does Standard Triple Therapy Still Have a Role in First-Line *Helicobacter pylori* Eradication in Korea?

Hye Kyung Jeon and Gwang Ha Kim

Department of Internal Medicine, Pusan National University School of Medicine, Busan, Korea

Helicobacter pylori infection is recognized as an important contributor to non-ulcer dyspepsia, peptic ulcer disease, gastric mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric cancer. Although the incidence of *H. pylori* infection has been decreasing owing to improvements in sanitation and living conditions, its prevalence remains high, especially in Asia. In Korea, the seroprevalence rate of *H. pylori* infection in asymptomatic adult subjects on health check-up was 59.6% in 2005 (1).

H. pylori eradication therapy is indicated for peptic ulcer diseases, early gastric cancer after endoscopic resection, and gastric MALT lymphoma in Korea. Recently, the eradication is frequently performed in subjects with upper gastrointestinal symptoms owing to the known relationship between *H. pylori* infection and gastric cancer. *H. pylori* eradication abolishes the inflammatory response and slows, or may arrest, the progression of atrophy. In addition, *H. pylori* eradication is effective in preventing gastric cancer, as the eradication treatment can be used to arrest the development of preneoplastic conditions, including atrophic gastritis and intestinal metaplasia. The adoption of *H. pylori* eradication therapy in Korea has increased owing to a deeper understanding of gastric diseases.

Triple therapy is used worldwide as the first-line treatment of *H. pylori* infection. This therapy utilizes a proton pump inhibitor (PPI), amoxicillin, and clarithromycin or metronidazole. As metronidazole-resistant *H. pylori* strains have been reported in at least 40% of clinical isolates, triple therapy with PPI, amoxicillin, and clarithromycin has become the standard regimen used for *H. pylori* eradication in Korea. However, recent data seem to suggest that this combination has lost some efficacy, with the highest reported curative response being 70%; less than the target cure rate of 80%, and far below that expected for therapeutic options for infectious diseases in general.

In the current issue of this journal, Gong et al. (2) reported the findings of a meta-analysis performed to evaluate the eradication rate of first-line standard triple therapy and thus validate current clinical practice in Korea. Following a systematic review of studies that used first-line triple therapy, a total of 104 studies were eligible for meta-analysis, including 38 randomized con-

trolled trials and 66 observational studies. A total of 42,124 subjects were included, and the sample size ranged from 12 to 4,198 subjects. The overall eradication rate with standard triple therapy was 76.4% (95% confident interval [CI], 72.1%-77.2%) in an intention-to-treat (ITT) analysis and 82.0% (95% CI, 80.8%-83.2%) in a per-protocol (PP) analysis.

A measurement of the eradication rate using ITT and PP analyses from the years 1998 to 2013 showed a decreasing trend over this study period ($P < 0.001$, both). In Korea, the clarithromycin resistance rate rapidly increased to 38.5% in 2009 (3). Therefore, primary resistance toward clarithromycin is hypothesized to be the most important factor influencing treatment failure. However, as Gong et al. (2) were unable to assess antibiotic resistance rates and exact compliance rates in each study population, other factors may be involved.

It is important to note that the eradication rate of the 7-day treatment quantified in this study was significantly lower than that of the 14-day treatment (81.1% vs 85.3%, $P < 0.001$). As such, longer treatment durations may prove more effective in curing infection. However, whether extending the duration of triple therapy from 7 to 10-14 days improves the eradication success is debatable. In a recent study, although the 7-day therapy was not inferior to the 14-day therapy, neither treatment protocol provided an acceptable eradication rate (90% in the PP analysis) (4).

While no new drugs have been developed for *H. pylori* eradication, a number of studies have been conducted in recent years to assess different combinations of known antibiotics. Much attention has been given to "sequential" and "concomitant" treatments. Sequential therapy typically consists of a 5-day course of PPI and amoxicillin, followed by a 5-day course of PPI, clarithromycin, and metronidazole or tinidazole. Concomitant therapy consists of a twice-daily dose of amoxicillin with clarithromycin, metronidazole, and PPI for 5 days. A recent study that utilized a meta-analysis to compare between the effectiveness of a 10-day sequential therapy and that of a 7-day standard triple therapy demonstrated the superiority of the 10-day sequential therapy for *H. pylori* eradication in Asian adults (5). Howev-

er, the pooled efficacy reported is lower than the published findings from earlier European studies. No significant difference in eradication rates was reported in a study comparing a 5-day concomitant therapy with a 7-day standard triple therapy (91.4% vs 86.1%, PP analysis) (6). In Korea, first-line *H. pylori* eradication approaches using sequential and concomitant therapies typically show suboptimal efficacies but have good patient compliance rates and no reports of serious adverse events. As antibiotics resistance has created a need for alternatives, either of these two regimens may be a reasonable option for the Korean population.

In conclusion, the results of the meta-analysis performed by Gong et al. (2) suggest that the *H. pylori* eradication rate achievable with standard triple therapy has decreased. Therefore, the development of novel therapeutic strategies to improve the first-line treatment of *H. pylori* infection is warranted in Korea. Prolonged treatment durations or other combination therapies may provide viable alternatives and should be investigated further.

ORCID

Hye Kyung Jeon <http://orcid.org/0000-0002-1550-7192>

Gwang Ha Kim <http://orcid.org/0000-0001-9721-5734>

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Address for Correspondence:

Gwang Ha Kim, MD

Department of Internal Medicine, Pusan National University School of Medicine,
Biomedical Research Institute, Pusan National University Hospital,
179 Gudeok-ro, Seo-gu, Busan 602-739, Korea
Tel: +82.51-240-7869, Fax: +82.51-244-8180
E-mail: doc0224@pusan.ac.kr