EDITORIAL

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Time to learn from the past and prepare for the future in *Helicobacter pylori* eradication

Chang Seok Bang and Gwang Ho Baik

Department of Internal Medicine, Hallym University College of Medicine, Chuncheon, Korea

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Helicobacter pylori is still prevalent in Korea, although the prevalence has decreased from 66.9% in 1998 to 54.4% in 2013 [1-5]. Sanitary improvements and wide application of eradication therapy have contributed to this. However, it is still a great socioeconomic and national healthcare burden [6]. This bacterial pathogen is involved in various gastrointestinal diseases, including gastritis, peptic ulcer, mucosa-associated lymphoid tissue lymphoma, and gastric cancer [7,8]. Although only 1% to 15% of patients with *H. pylori* infection develop the clinical disease, even asymptomatic *H. pylori* gastritis should be considered an infectious disease and treated to prevent severe complications, such as gastric cancer, as reported by the Kyoto Global Consensus conference [4]. This suggests a paradigm shift in the eradication of *H. pylori* from treatment to prevention [4].

Standard triple therapy (standard dose proton pump inhibitor, amoxicillin 1 g, and clarithromycin 500 mg twice daily for 7 to 14 days) is the recommended first-line regimen for eradication of *H. pylori* in Korea [9]. Over the past decade, studies of the trend in *H. pylori* eradication rates in Korea have shown a constant or decreasing trend [10]. Concerns about changing the first-line regimen have been growing, because studies indicating a constant trend also showed eradication rates below 90% in per-protocol analyses [10]. Particularly, a recent meta-analysis revealed a decreasing trend in the eradication rate (from 1998 to 2013) in Korea, which has an overall eradication rate of 74.6% (95% confidence interval [CI], 72.1 to 77.2) with intention-to-treat and 82.0% (95% CI, 80.8 to 83.2) by per-protocol analysis [11].

In this issue, Kim et al. [12] reported a trend in the *H. pylori* eradication rate using first-line triple therapy in Metropolitan Busan, which is the second largest city in Korea after Seoul. This retrospective study included 1,413 patients who were treated with the standard triple regimen for 7 days between 2003 and 2012 [12]. The overall eradication rate was 84.9% (per-protocol analysis), which is an unacceptable level for the currently recommended regimen. Moreover, the most recent eradication rate was 78.8% in 2012, which has decreased significantly during the last 10 years [12]. These results are consistent with those of the recent meta-analysis and indicate the need for a novel therapeutic regimen in Korea. If the treatment duration had been extended to 14 days, the expected improvement in the eradication rate would have been approximately 5%, which is still an unacceptable level [13].

High clarithromycin resistance in

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Correspondence to
Gwang Ho Baik, M.D.
Department of Internal Medicine, Hallym University Chuncheon Sacred Heart Hospital, 77 Sakju-ro, Chuncheon 24253, Korea
Tel: +82-33-240-5821
Fax: +82-33-241-8064
E-mail: baikgh@hallym.or.kr

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Korea is suspected to be a cause of treatment failure. Although data are scarce, the clarithromycin resistance rate was estimated to be 17.2% to 23.7% in 2012 [14]. Another study reported a resistance rate of 38.5% in 2009, which falls into the category of high clarithromycin resistance [13,15]. The Korean guideline recommends a bismuth-containing quadruple regimen (standard dose proton pump inhibitor twice daily, metronidazole 500 mg three times daily, and bismuth 120 mg and tetracycline 500 mg four times daily for 7 to 14 days) in areas where clarithromycin resistance is high [9]. It is difficult to determine when to change the first-line regimen in an area, because only a few studies have reported data on antibiotic resistance in *H. pylori* eradication. However, time trend data continuously indicate the need for a novel regimen. If possible, a susceptibility test-based combination of drugs is the ideal regimen for eradication of an infectious pathogen. However, it is nearly impossible to perform culture and susceptibility tests for *H. pylori* in hospitals. With the increase in geographical antibiotic resistance data, it should be possible to determine the preferred regimen among the potential candidates according to the geographic area.

Kim et al. [12] also reported that smoking and female gender are associated with treatment failure. Smoking is a well-known risk factor for treatment failure. As the authors described, a reduction in antibiotic delivery due to decreased gastric blood flow is suspected to be the main mechanism [13]. However, it is not clear why female gender is associated with treatment failure. The high prevalence of *H. pylori* infection in carriers of the A2143G mutation in 23S rRNA, which is associated with treatment failure, is presumed to be a possible cause [12,16]. However, another Korean study did not show a preponderance of the A2143G mutation in women [17].

In brief, time trend data indicate decreasing efficacy of standard triple therapy in the eradication of *H. pylori*. However, no superior regimen has been found to be more effective than standard triple therapy in Korea. The combination of existing drugs, based on the results of antibiotic susceptibility tests, is the ideal method. Without geographic antibiotic resistance data, it is impossible to compare or interpret the clinical trials of novel regimens [18]. In the setting of a culture and susceptibility test-based regimen choice or with the accumulation of local antibiotic resistance data, it may be possible to determine the best regimen or find novel therapies.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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