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Research note

Primary antibiotic resistance of *Helicobacter pylori* in Chinese patients: a multiregion prospective 7-year study

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ABSTRACT

Objectives: To explore the characteristics of *Helicobacter pylori* resistance in China and the association between antibiotic resistance and several clinical factors.
Methods: *H. pylori* strains were collected from patients in 13 provinces or cities in China between 2010 and 2016. Demographic data including type of disease, geographic area, age, gender and isolation year were collected to analyse their association with antibiotic resistance. Antibiotic resistance was detected using the Etest test and the Kirby-Bauer disc diffusion method.
Results: *H. pylori* were successfully cultured from 1117 patients. The prevalence of metronidazole, clarithromycin (CLA), azithromycin, levofloxacin (LEV), moxifloxacin, amoxicillin (AMO), tetracycline and rifampicin resistance was 78.2, 22.1, 23.3, 19.2, 17.2, 3.4, 1.9 and 1.5%, respectively. No resistance to furazolidone was observed. The resistance rates to LEV and moxifloxacin were higher in strains isolated from patients with gastritis compared to those with duodenal ulcer and among women. Compared to patients ≥40 years old, younger patients exhibited lower resistance rates to CLA, azithromycin, LEV and moxifloxacin. The resistance rates to CLA and AMO were higher in strains isolated more recently, and we also found that the prevalence of resistance to metronidazole, CLA, azithromycin and AMO were significantly different among different regions of China.

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Conclusions: The resistance rates to metronidazole, CLA and LEV were high in China. Patient age, gender, disease and location were associated with the resistance of *H. pylori* to some antibiotics. Furazolidone, AMO and tetracycline are better choices for *H. pylori* treatment in China. **D.-S. Liu, Clin Microbiol Infect 2018;24:780.e5–780.e8**

Introduction

Helicobacter pylori plays an important role in some gastrointestinal diseases, such as peptic ulcers, chronic gastritis and gastric adenocarcinoma [1,2]. To achieve a higher eradication rate, an empirical therapy recommended as primary treatment must be established on the basis of local antibiotic resistance characteristics [3].

China has a large *H. pylori*–infected population that exhibits complicated antibiotic resistance features [4]. Several studies have reported antibiotic resistance in some regions of China. For instance, Song *et al.* [5] examined the resistance patterns of *H. pylori* isolated from patients in four cities and found high clarithromycin (CLA), levofloxacin (LEV) and rifampicin (RIF) resistance between 2008 and 2012, and the resistance rate to metronidazole (MET) in the southeast coastal province of China was 95.4% [6]. As a result of the prevalence of high resistance rates for MET and CLA in most area of China, bismuth-containing quadruple therapy was the recommended first-line treatment for *H. pylori* eradication in the latest consensus report of *H. pylori* infection in China, and seven antibiotic combinations used in bismuth-containing quadruple therapy are also suggested in the consensus [7].

Because dynamic monitoring of resistance rates is important for eradication treatment, we performed a survey of *H. pylori* antibiotic resistance from 2010 to 2016 in 13 provinces or cities of China and analysed *H. pylori* resistance characteristics. In addition, we investigated the correlation between antibiotic resistance and several clinical factors.

Materials and methods

Patients and H. pylori strains

H. pylori strains were collected from patients undergoing upper gastrointestinal endoscopy in 18 hospitals between 2010 and 2016. Adult patients were included if they had not received treatment for *H. pylori* infection previously. Patients receiving antibiotics, proton-pump inhibitors, H_2 receptor blockers or bismuth salts within 4 weeks of the endoscopy were excluded. The demographic data included the type of disease, geographic area, patient age and gender, and the year the sample was collected. Informed consent was obtained from all participants. The protocol was approved by the ethics committee of the First Affiliated Hospital of Nanchang University (IRB2011002).

For *H. pylori* culture, biopsy samples were homogenized and cultured on *Campylobacter* agar (Oxoid, Basingstoke, UK) supplemented with 5% sheep's blood (Bio-kont, Zhejiang, China) containing vancomycin, trimethoprim, polymyxin B and amphotericin B (Duly Biotech, Nanjing, China). The plates were incubated at 37°C under microaerophilic conditions (10% CO_2, 5% O_2 and 85% N_2) in a humid atmosphere for 3 to 5 days.

Antibiotic susceptibility test

An Etest (bioMérieux, Marcy l'Etoile, France) was used to determine the minimum inhibitory concentrations (MIC) of amoxicillin (AMO), MET, CLA, LEV, azithromycin (AZI), moxifloxacin (MOX), RIF and tetracycline (TET). The Kirby-Bauer disc diffusion method (Oxoid) was used to determine the inhibition zone for furazolidone (FUR). A strain was considered resistant if the MIC >1 μg/mL for AMO, ≥1 μg/mL for CLA and AZI, >2 μg/mL for TET, >4 μg/mL for MET (http://www.biomerieux-usa.com/sites/subsidiary_us/files/supplementary_inserts_-_16273_-_b_-_en_-_eag_-_etest_application_guide-3.pdf), MIC >1 μg/mL for LEV, MOX and RIF (http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/Breakpoint_table_v_3.1.pdf) and if the inhibition zone was <7 mm for FUR [8]. *H. pylori* strain ATCC 43504 was included as an antibiotic susceptibility testing quality control. All antibiotic susceptibility tests were conducted at the Institute of Gastroenterology and Hepatology, First Affiliated Hospital of Nanchang University.

Statistical analysis

Data analysis was performed by SPSS 17.0 (IBM SPSS, Chicago, IL, USA). Frequencies and percentages were used to describe the antibiotic resistance rates of *H. pylori* isolates. The univariate association between each factor was quantified by Fisher's exact test and the chi-square test. A probability value of <0.05 from a two-tailed test was considered statistically significant.

Results

Overall H. pylori antibiotic resistance

Of the 1117 *H. pylori* strains, 960 strains completed susceptibility testing for nine antibiotics, whereas 157 strains completed susceptibility testing for eight antibiotics (except for FUR). The prevalence of *H. pylori* resistance is shown in Table 1. The resistance rates to MET, CLA, AZI, LEV, MOX, AMO, TET, RIF and FUR were 78.2, 22.1, 23.3, 19.2, 17.2, 3.4, 1.9, 1.5 and 0%, respectively. On the other hand, we also compared four antibiotic combinations among MET, CLA, LEV and seven antibiotic combinations used in bismuth-containing quadruple therapy recommend in the fifth Chinese national consensus report on the management of *H. pylori* infection. In general, the antibiotic combinations consisting of MET, CLA and LEV had higher combined resistance rate, and the antibiotic combinations recommended in bismuth-containing quadruple therapy had lower combined resistance rates. Results are depicted in Fig. 1.

Factors associated with antibiotic resistance

The analysis revealed that compared to men, women had a significantly higher resistance rate to LEV (p 0.016) and MOX