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Editorial

Noninvasive diagnostic methods for *Helicobacter pylori* infection

Helicobacter pylori is one of the most frequently occurring and persistent bacterial infections worldwide. *H. pylori* bacteria are associated with peptic ulcer disease, mucosa-associated lymphoid tissue lymphoma, and gastric cancer.[1] Various diagnostic methods are used to detect *H. pylori* infection. However, only highly accurate tests with 90% sensitivity and 90% specificity should be used in clinical practice. Commonly, the invasive diagnostic methods include endoscopy with histology, rapid urease test, bacterial culture, and molecular method (such as polymerase chain reaction); the noninvasive methods include serology, urea breath test, and stool antigen test (SAT). The use of a saliva antigen or antibody test for *H. pylori* detection remains premature.[2] Herein, we briefly review these noninvasive diagnostic methods.

The 13 C-urea breath test (13C-UBT) is one of the most reliable tests for diagnosing *H. pylori* infection. It is a simple, noninvasive, and safe test that provides excellent accuracy both for the initial diagnosis of *H. pylori* infection and for the confirmation of its eradication.[3] Posttreatment UBT is usually performed 4−6 weeks after the eradication therapy. With the most widely used protocol (75 mg of urea with citric acid), excellent accuracy is obtained when breath samples are collected as early as 15 minutes after urea ingestion. The 13C-UBT in adults has a high sensitivity (88−95%) and specificity (95−100%).[4] However, the test has shown heterogeneous accuracy in the pediatric population, especially in young children.

The SAT is a noninvasive method used to detect *H. pylori*, usually recommended when UBT is not available. This method is especially relevant for children's access to a safe diagnosis. There are two types of SATs used for *H. pylori* detection: the enzyme immunoassay and an assay based on immunochromatography. A meta-analysis revealed that the global sensitivity and specificity of SATs are 94% and 97%, respectively.[5] *H. pylori* SAT (easy One-Step Test, Firstep Bioresearch Inc., Tainan, Taiwan) was added to the fecal occult blood test used for colorectal cancer screening in a program in Taiwan in order to detect upper gastrointestinal (GI) lesions, mostly due to *H. pylori*. The prevalence of upper GI lesions was higher in those patients with a positive *H. pylori* SAT than in those with a positive guaiac-based test (34.6% vs. 24.7%).[6]

Detecting anti-*H. pylori* antibodies [immunoglobulin G (IgG)] with enzyme-linked immunosorbent assay through routine serology is recommended for initial screening, requiring further confirmation by histology and/or culture prior to treatment. Serological tests have several advantages, in that they are noninvasive and they do not produce false negative results in patients receiving certain treatments (proton pump inhibitors and antibiotics) or presenting with acute bleeding. It also can detect specific *H. pylori* proteins (with virulence factors such as Cag A, Vac A). One drawback is the prolonged existence of antibodies in the host even after a successful eradication therapy. This situation limits the utility of serology in confirming the eradication of *H. pylori*. A recent study with 29 different serological tests showed sensitivity rates ranging from 55.6% to 100%, and specificity rates ranging from 59.6% to 97.9 %.[7]

Detection of *H. pylori* in other specimens includes saliva, subgingival biofilm, dental plaque, and gastric juice. The ability to detect *H. pylori* antibodies in saliva is lower than in blood-based serology. However, the use of molecular techniques for the detection of *H. pylori* infection in saliva or dental plaque may make these specimens attractive because they are easier to collect. The prevalence of *H. pylori* in dental plaques has been reported by several studies, with findings ranging from 0% to 100%.[8] This wide variation may be explained by the characteristics of the different sample populations, differing sampling procedures, and differing methodologies used to detect *H. pylori* in dental plaque. Compared with studies on dental plaque, there are fewer reports on the prevalence of *H. pylori* detection in saliva, and the majority of these studies used either culture or polymerase chain reaction methods. Ultimately, the detection rates in saliva were generally noted to be less than those in dental plaque.[8] This may be because as a biofilm, dental plaque allows the bacteria to adhere to solid surfaces, and the constant flow of saliva may contribute to a reduction in bacterial load, making detection difficult. A study detecting anti-*H. pylori* IgG by enzyme-linked immunosorbent assay in India showed a 79% sensitivity and a 64% specificity, with 75% accuracy.[9] Another study detecting *H. pylori* saliva antigen suggested that oral *H. pylori* infection continued to persist even though gastric *H. pylori* was already cured (negative UBT).[10] Yang et al's[2] study, in this issue, showed that the one-step *H. pylori* saliva antigen test exhibited a moderate sensitivity (71%) but low specificity (55%). The detection of *H. pylori* in saliva and dental plaque may precede or may be independent of gastric infection. It is not yet clear whether the presence of *H. pylori* in the oral cavity represents long-term

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colonization or whether its presence is transient due to either gastric reflux or because it is in route to the stomach.[8]

In conclusion, 13C-UBT is one of the most reliable tests for diagnosing *H. pylori* infection, especially after eradication therapy. The SAT method is recommended for children. It could be combined with a stool occult blood test (enzyme immunoassay) for upper GI screening and colorectal cancer screening, respectively. However, additional study is necessary to help determine the overall accuracy and clinical implications when *H. Pylori* is detected in saliva or dental plaques.

Conflicts of interest

The author declares that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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