Helicobacter Pylon: what test for Diagnosis and what Treatment for Eradication?

T. S. Abidi (Department of Anatomy,Edward Medical College, Lahore.)

Diagnosis and treatment of peptic ulcer disease has been revolutionized after the isolation of Helicobacter pylori (H. pylon). Peptic ulcer is now approached as an infectious disease. Several mysteries have been solved related to H. pylon but two fundamental concerns are still unresolved for practical management of H. pylori infection.

What is the ideal reliable and cost effective test to diagnose H.pylori infection?

Diagnostic test for H.pylori are either non-invasive or invasive by endoscopic biopsy of gastric mucosa. Selection of appropriate test depends on the clinical setting.[1] Noninvasive methods include urea breath test (UBT), serological test and stool antigen assay (H. pylon SA).

UBT relies on the amount of H.pylori derived urease activities in the stomach. This test quantitatively detects active infection with a sensitivity and specificity of more than 90%. UBI' is also a test to validate cure from H.pylori infection if repeated 4-8weeks after eradication therapy for H.pylori. It is considered as the gold standard "reference test" to validate diagnosis of H.pylori infection through any other test.[2] Unfortunately this is expensive and not available iii Pakistan.

H. pylon serological testing is cheap and widely used for the diagnosis of H.pylori infection in patients before treatment. It is highly sensitive and specific similar to UBT if serology is performed in a laboratory setup. This test should be performed with proper cut-off values based upon the local prevalence data of H.pylori infection in the region. Serological test may give inconsistent results in office based setting.[3] it has limited value in determining the success of therapy and is not reliable in young children. A new variant with marker of current infection (CIM) may be more sensitive in diagnosing the active H.pylori infection.[4] In a patient with dyspepsia in primary care setting. the test and treatment strategy for H.pylori infection has been shown in several reports to be reasonable.[5] Serological test will serve the purpose in this context by rapid lion-invasive diagnosis. This test can also be used to rule out H.pylori infection when the diagnosis would other wise make a major difference to a patient's management and UBT is not the test of choice. For example UBT may be normal in patients with bleeding peptic ulcer treated with antibiotics.However a high titre of H.pylori antibody is justified to start anti H.pylori treatment.[6] On the other hand an interesting point has been raised in a study by Abbas et al (reference this issue of the journal) indicating positive antibody titer in patients with duodenal ulceration with normal urea breath test. This simply reflects the fact that antibody titer remained elevated for a long time after the disappearance of H.pylori infection. A positive ll.pvlori serology does not necessarily mean active H. pylon infection even in the setting of documented duodenal ulceration.

Stool antigen test for H.pylori seems to be a true alternative to UBT with sensitivity of 89-98°/o and a specificity of over 90%.[7] Stool test is also a suitable investigation for confirming cure in the follow-up of patients after the eradication of H. pylon infection. Large prospective validations studies are still required considering the reference tests as gold standard and cut-off value used for spectrophotometric H.pylori SA readings based

upon regional data.[8]
Patients with alarming symptoms such as anemia, gastrointestinal bleeding or weight loss and patients of advanced age with dyspeptic symptoms should undergo gastroscopy. Urease test on antral biopsy is a rapid and cheap test with sensitivity of 95%and a specificity of 98%.[9] Histology and staining for H.pylori is not required in clinical practice if urease test is positive on gastric biopsy for the management of H. pylori infection. Culture for H.pylori is not routinely performed. However this is indicated in those individuals who had failed to eradicate H.pylori.[10] Moreover antibiotic susceptibility against H.pylori has also recently been standardized.[11]
What would be the appropriate treatment for eradication of H. pylon?
The goal of the treatment is the complete elimination of the organism. Once this has been achieved the benefit of the treatment is long-lasting with low re-infection rate. In clinical practice one must use only those regimens which have at least 80% H. pylori eradication rate without much side effects and with minimal induction of bacterial resistance. To achieve these goals a combination of antibiotics along with proton pump inhibitors or ranitidine bismith citrate are the best and time tested choices. The appropriate combination of antibiotics and duration of therapy are however the two major issues. A combination of two or more antimicrobial agents increases the rate of cure. The chief antimicrobials used in these combinations are amoxicillin, clarithromycin, metronidazole, tetracycline and bismuth. Primary resistance to amoxicillin and tertracycline remains uncommon but the frequency of resistance to clarithromycin is now at least 10% or even higher in certain countries.[12] Metronidazole resistance ranges between 20-30%[12] and is expected to be more frequent in developing countries including Pakistan because of its frequent use in treatment of several other diseases. Study by Abbas et al (published in this issue)of the journal is relevant to situation in our country, where a high resistance of metronidazole is expected against H. pylon because of its overwhelming use. In this context substitution of metronidazole by tinadozole can be considered. However, clarithromycin and rnetronidazole are the major antibiotics against H. pylon. A combination of both clarithrornycin and nitroimadazole are usually no more effective than regimens with only one of these antibiotics. Considering the serious problems of resistance to H. pylon, it has been suggested that both key antibiotics (clarithromycin and metronidazole) should not be used together in majority of cases with H. pylon infection especially as first line therapy.[13]
Common first line therapy for eradication of H. pylon are the combination of one of the proton pump inhibitors (orneprazo le, lansoprazole, esorneprazole, pantoprazole) or ranitidine bismith citrate with clanithromycin and amoxicillin. Some other novel combination like ranitidine bismith citrate with furazolidone may also be considered.[14] In a study done in Bangladesh 100°/a eradication was achieved when bismuth subcitrate was used in combination with furazolidine and am ox ic ill in.[15]
Duration of the therapy remains controversial. In a recent meta analysis. [14] day treatment cure rate was 7-9 percentage point better than 7-day treatment.[16] Duration of anti H. pylon treatment should be determined according to the local resistance pattern of antibiotics against H.pylori. In our study on eradication of H. pylon omeprazole, amoxicillin and clanithnomycin given to patients with duodenal ulcer for a week was found to have an eradication rate of 85%)[17]
Testing for H. pylon is thus recommended only in those cases where treatment is planned

or when there is a necessity to determine local prevalence of H.pylori.. The best choice would be a non-invasive test. In Pakistan a serological test or H. pylon SA are the best choices with some limitations. Choice of antibiotic should be based upon local prevalence of animicrobial resistance. In order to recommend a regimen based on clarithromycin or metronidazole or lurazolidine, further studies need to be conducted in the context of Pakistan. The range of duration of therapy (7-14 days) is still controversial. It may however, be noted that the duration may be even longer in certain subsets of patients. Local studies are required to validate the ideal test for diagnosis and most appropriate treatment regimen to follow for eradication of H. pylon in future.

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