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Research Article

Comparison between rapid urease test and carbon 14 urea breath test in the diagnosis of Helicobacter pylori infection

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ABSTRACT

Background: The most common human infection of upper gastrointestinal region is *Helicobacter pylori*. Most individuals remain asymptomatic due to misuse of antibiotic and proton pump inhibitors.
Methods: 50 patients admitted or on outpatient department basis were selected based on the upper gastrointestinal symptoms and whether they were 18 years and above.
Results: The Rapid Urease Test (RUT) had 84% sensitivity and 91% specificity, with an overall accuracy of 88%. The results of the Urea breath Test (UBT) showed 88% sensitivity and 83% specificity, and an overall accuracy of 85%.
Conclusions: The invasive procedure OGD scopy need not be done in patients for the sole purpose of diagnosing HP infection as the diagnostic efficacies of RUT & UBT tests are similar.

Keywords: Rapid urease test, Carbon 14 urea breath test, Helicobacter pylori, Peptic ulcer

INTRODUCTION

Helicobacter pylorus (*H. pylori*) is the most common human infection. Though most individuals are asymptomatic, *H. pylori* plays a key role in the aetiology of many upper gastrointestinal disorders. It is well known that *H. pylori* infection of the gastro duodenal mucosa causes chronic active gastritis and may dispose to peptic ulcer disease. Many a times the diagnosis may be missed due to rampant misuse of antibiotics and proton pump inhibitors. Eradication of *H. pylori* infection substantially reduces the frequency of peptic ulcer recurrence. Several invasive and non-invasive methods to detect *H. pylori* infection of the stomach have been described in the literature. Until recently, the practice has mainly been focused on the detection of *H. pylori* by endoscopic biopsy of the gastric mucosa. Early treatment for gastric *H. pylori* infection can prevent the later development of gastric carcinoma. Thus diagnosis and treatment of *H. pylori* infection are of great importance worldwide. This study was done to compare two diagnostic tests and to evaluate if the upcoming and non-invasive Urea Breath Test (UBT) is as effective as Rapid Urease Test (RUT) in the diagnosis of HP infection.

Oesophagogastroduodenoscopy: (Olympus Evis Exera II 180 model). The endoscopic examination is done on the patients fasting overnight. The procedure is explained to the patients and valid informed and written consent is taken. 10% xylocaine solution is sprayed in the oropharynx and over posterior pharyngeal wall few minutes before the procedure. The examination is done in left lateral position with thighs and knee flexed. Artificial dentures, if present are removed. A guard is placed between teeth to protect tongue, teeth as well as the endoscope. The tip of endoscope is placed at the crico-

pharyngeal sphincter of the oesophagus and patient is encouraged to swallow while gentle pressure is exerted, small amount of air is passed through the endoscope to visualise the oesophageal lumen. The endoscope was then passed under direct vision into the stomach. The instrument tip is retroflexed in the stomach to visualise gastric cardia, the fundus and whole of the lesser curvature. The pylorus is traversed and first and second portion of duodenum is visualised. Two or more antral biopsies are taken and biopsy specimens were subjected to the rapid urease test kit. Diagnostic upper GI endoscopy is a remarkably safe procedure.

Rapid urease test: (PRONTO DRY kit, Mfd. by Matack, Switzerland). The rapid urease test is the most widely used standard procedure for the detection of *H. pylori* infection. This is because it is a simple, reliable and inexpensive test, which provides results rapidly. Each kit is a plastic slide having a blister in its middle which was filled with urea mixed with pH indicator. This mixture was in gel form and was sealed inside the blister. The indicator was yellow in colour giving the gel its yellow colour and when exposed to alkaline media it has the property to turn red/ pink. The biopsy material was placed inside the blister pack with sterile water and it was resealed. It was observed for next two hours and any change in colour was noted. Presence of urease in the biopsy material cause hydrolysis of urea inside the kit forming ammonium hydroxide which being alkaline changes the colour of indicator from yellow to red. This provided indirect evidence of presence of urease producing organism *H. pylori* in the biopsy material.

Urea breath test: (Heliprobe, Mfd by Kibion, Sweden). On an empty stomach the patient swallows a HeliCapTM capsule with a glass of water. HeliCapTM, containing 14C-labeled urea, disintegrates rapidly in the stomach and the 1C-urea is dissolved. In the presence of *H. pylori*, the 1C-urea is metabolized to carbon dioxide and ammonia by the enzyme urease, produced by *H. pylori*. The available 1C isotopes, now in the form of $1CO_2$, diffuse into the blood to be transported to the lungs, where it is exhaled in the breath to be captured during sampling. A positive answer offers conclusive evidence that the patient is infected with *H. pylori*. In the absence of *H. pylori*, the administered urea is absorbed in the gastrointestinal tract and subsequently voided. Results are expressed as 0 = patient not infected, 1 = borderline, 2 = patient infected C14 is a β-emitter and the maximum β range in plastic is only 0.25 mm. Since HeliCapTM capsules are stored in plastic containers, there is no radioactivity at all outside the package. Therefore, no special shielding or protection is required when shipping HeliCapTM capsules as there is no risk of exposure to radiation from the capsules.

METHODS

This study was conducted at our hospital on 50 subjects, admitted or on OPD basis over a period of 1 year from Dec 2013 to Dec 2014. A thorough history, examination of the patient, basic necessary blood investigations, to rule out other causes of dyspepsia and oesophagogastroduodenoscopy was done on patients. Biopsies were taken from the antrum of the stomach and tested for RUT. All patients tested positive for RUT was then subjected to UBT. Anti *H. pylori* treatment was given to all positive patients. Follow up was done after two weeks and resolution of symptoms was noted.

Inclusion criteria

>18 years of age and upper GI symptoms (Any: nausea/vomiting, epigastric pain, morning hunger pains, heartburn).

Exclusion criteria

Pregnancy in females, Intake of PPIs, Bismuth compounds, antibiotics (All classes except: vancomycin, nalidixic acid, trimethoprim, amphotericin B), H2RA in the last 30 days, known cases of HP infection, patients who have previously taken treatment for the same, Patients with bleeding disorders, anti-coagulant therapy and CKD/Liver cirrhosis.

RESULTS

We used the gastric antral biopsy as the reference value (gold standard) for comparison with the two other methods. Of the 50 gastric biopsies, 26 were positive for *H. pylori*, and 24 were negative. Of the 26 patient's positive on histopathology, 22 were positive in the RUT and 23 patients were positive in the UBT. Of the 24 patients with negative histopathology for *H. pylori*, 22 were negative in the RUT and 20 were negative in the UBT. Using the histopathology as the gold standard, the RUT had 84% sensitivity and 91% specificity, with an overall accuracy of 88%. The results of the UBT showed 88% sensitivity and 83% specificity, and an overall accuracy of 85% (Table 1).

Table 1: Using histopathology as gold standard, reliability of RUT and carbon-14 urea breath test is as follows.

	RUT	C-14 UBT
Sensitivity test	84%	88%
Specificity	91%	83%
Positive predictive value	91%	85%
Negative predictive value	85%	86%
Overall accuracy	88%	85%

DISCUSSION

There have been a variety of publications describing the results of various methods of diagnosing *H. pylori* infection. Graham et al. were the first to report the use of a breath test for the detection of gastric urease activity.[1]

Recent modifications have included the use of carbon-14-labeled urea, the use of lower doses of radio-labelled urea, and corrections for the rates of carbon dioxide (CO_2) production based on the patient's weight.[2] Junaitis et al.[3] in their study proved that the diagnostic values of "Heliprobe" assuming the *H. pylori* positivity, if the results of two tests (rapid urease test and histology) are positive, were: sensitivity - 97%, specificity - 87%, positive predictive value - 93%, negative predictive value - 95%, accuracy - 94%. The diagnostic values of "Heliprobe" assuming the *H. pylori* positivity, if at least the results of one test are positive: sensitivity - 92%, specificity - 100%, positive predictive value - 100%, negative predictive value - 84%, accuracy - 94%. Abrams et al.[4] reported that testing the biopsy sample for the presence of urease is a much simpler, quicker and less expensive test than either culture or histology and has high sensitivity (90 to 95 %) and specificity (98 to 100%). However, a biopsy sample is still required. The (14C) carbon urea breath test is sensitive, non-invasive tests which can be used to determine the presence of *H. pylori* prior to initial treatment and for follow up after antibiotic therapy. Al-Fadda et al.[5] in their study using the histopathology as the gold standard, the RUT had an 88% sensitivity and 87% specificity, with an overall accuracy of 88%. The results of the UBT showed 85% sensitivity and 70% specificity, and an overall accuracy of 78%. They concluded that C-14-urea breath testing is a safe, simple, inexpensive method of accurately detecting *H. pylori* infection, yielding results which are comparable to those obtained using RUT at endoscopy as well as actual pathological examination of biopsy specimens. Rasool et al.[6] compared the cost and validity of UBT and found that Microdose 14C UBT was comparable to histology and rapid urease test and that C14 UBT is an economical, self-sufficient and suitable test to diagnose active *H. pylori* infection in less developed countries. Although there are no recent high quality prospective studies of complications following diagnostic upper GI endoscopy, one large US study estimated an overall complication rate (including mucosal biopsy) of 0.13% and an associated mortality of 0.004%.[7]

The radiation exposure from a 1-µCi dose of 14C HeliCapTM capsules is estimated to be equivalent to the amount of radiation received by the patient from the natural environment over a period of 11 hours[4] and is one tenth the amount of radiation that is received in a plain chest X-ray.[8] It has been recognized that *H. pylori*-infected individuals have a twofold increased risk of developing gastroduodenal complications while taking NSAIDs including aspirin.[9]

Apart from *H. pylori*, diverse factors such as mucosal changes, acid secretion, alcohol, and NSAIDs have been reported to be involved. The UBT indirectly detects gastric HP by measuring urease activity. However, urease-producing bacteria are also present in the oropharynx and may cause false positive results, especially in early breath samples. Late breath sampling may result in false-negative results because of emptying of urea from the stomach. Several procedures to avoid contamination of breath by the oropharyngeal flora have been suggested, including mouth washing, simultaneous meal to delay gastric emptying, and performance of multiple breath sampling. This can be bypassed by using 14C-urea in a gelatine capsule. Hamlet et al reported that when the 14C-urea is supplied in a capsule, a single 10-min breath sample is highly accurate (100% sensitivity and specificity) for the diagnosis of HP infection. They compared the capsule method with the urea drink method and found the former to be more reliable because no overlapping in activity occurred between HP-positive and -negative patients; by contrast, conventional breath testing showed overlapping during the whole 30-min test period. Their study also showed that a fatty test meal lowers the $14CO_2$ excretion during the first 20 min and may adversely affect the accuracy of a rapid UBT.[10] A large number of investigators have reported that the UBT becomes false negative during therapy with proton pump inhibitors, lansoprazole, bismuth compounds, antibiotics and ranitidine.[11-13]

14C has a physical half-life of about 5000 years, raising the question of the risks of radiation exposure. Because nearly the entire ingested isotope is rapidly excreted in urine or breath over the following 72 h and only a small amount of isotope is used, the test actually entails low radiation exposure (3 µSv).[14,15]

In fact, the dose is less than the natural background radiation in one day. As mentioned by Boivin et al., the debate on safety has revolved only around the radiation dose received from 14C UBT, and it has been generally accepted that there is no or a lower risk with the 13C alternative. On the other hand, 13C-UBT contains more than 30000 times as much urea as 14C-UBT, and the safety of this amount of urea is also questionable.[16] For this reason, in 1997 the Nuclear Regulatory Commission permitted *in vivo* diagnostic use of capsules containing 1 µCi of 14C-urea without a license.[17]

CONCLUSION

Urea breath test is a bedside simple, rapid, practical, safe, cheap, non-invasive, quick test and highly accurate system for the diagnosis of HP infection. The main advantages are commercial availability, no risk of spills, reduced interference by oropharyngeal flora, shorter test duration, low radiation dose, simple and safe breath collection, and a practical and cheap counting system and this research study has proved that OGD scopy need not be done in patients for the sole purpose of diagnosing HP infection as the diagnostic efficacies of these two tests are similar.

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