Nuclear Medicine's New Role in Peptic Ulcer Disease Management

James Corley, Jeannie Yoder, Sandra Raibon and George Burke

Department of Radiology, Medical College of Georgia, Augusta, Georgia

This article describes the new developments in managing peptic ulcer disease. We discuss the role Heliocobactor pylori plays in peptic ulcer disease patients and how the presence of the organism is detected. The ^{14}C urea breath test can serve as an important diagnostic tool in detecting the organism associated with peptic ulcer.

Key Words: peptic ulcer; Heliocobactor pylori; carbon-14 urea breath test

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The management of peptic ulcer disease may soon undergo a significant change with the introduction of a new nuclear medicine diagnostic test. The discovery of Heliocobactor pylori (H. pylori) and its significance in antral gastritis and duodenal ulceration has caused a dramatic change in the understanding and treatment of peptic ulcer disease during the past decade (*1*).

A new diagnostic radiopharmaceutical, ^{14}C urea, promises to be a useful noninvasive method for the detection of H. pylori, an organism implicated in the pathogenesis of gastritis and peptic ulcer. Previously endoscopy has played an important role in the management of peptic ulcer disease because it is primarily a mucosal lesion. This invasive procedure may soon be replaced with a simple noninvasive test which has proven to be sensitive, specific and low in cost during early clinical trials.

HELIOCOBACTOR PYLORI

Marshall and Warren were the first to associate a spiral urease-producing organism from the stomachs of patients with gastritis and peptic ulceration (*2*). This organism was later identified as H. pylori. The gastric mucus layer of the human stomach is the natural habitat for this spiral-shaped bacillus seen on Giemsa stain. H. pylori is found in association with active chronic gastritis and is probably the most common cause of nonautoimmune gastritis. Most patients who have duodenal ulcers also have chronic antral gastritis. The presence of gastric acid is still a necessary part of the pathogenesis of ulcers, but its role is likely limited to the contribution to the consequence of H. pylori infection, except in Zollinger-Ellison syndrome.

H. pylori produces urease, an enzyme that is only rarely found in mammalian cells. This enzyme is capable of converting urea into ammonium and bicarbonate:

$$\underset{\text{Urea}}{CO(HN_2)_2} + 2H_2O + H^+ \xrightarrow{\text{Urease}} \underset{\text{Ammonium}}{2NH_4^+} + \underset{\text{Bicarbonate}}{HCO_3^-}$$

The HCO_3^- enters the blood stream, is carried to the lungs and is rapidly excreted from the lungs as CO_2. If urea manufactured with radioactive carbon (^{14}C) is administered to a patient, $^{14}CO_2$ detected in the breath indicates urease was present in the patient's stomach. In patients with H. pylori, $^{14}CO_2$ is usually detectable in the breath 5 min after administration with peak excretion between 10 and 15 min. H. pylori contains an abundance of urease and is one of only a few organisms that can reside in the human stomach.

There are both invasive and noninvasive measures for detecting the presence of H. pylori. Although long considered the gold standard, a biopsy of the gastric mucosa requires endoscopy which limits its usefulness. Studies show that nearly all patients colonized with H. pylori had antral gastritis and eradication of H. pylori infection resulted in the resolution of gastritis in greater than 90% of patients (*1*). Serological testing detected antibodies to H. pylori with a specificity of greater than 90% in patients who were infected with the bacterium (*3*). However, this test cannot be used to confirm eradication of the organism because of the slow decline of the antibody titer after successful treatment (*1*).

MATERIALS AND METHODS

Carbon-14-labeled urea was supplied in a gelatin capsule containing 1 μCi (37 kBq) of the radiopharmaceutical. Currently this is an investigational drug which is undergoing Phase III FDA evaluation (Tri-Med Specialties, Charlottesville, VA).

The preparation of the patient included fasting for 6 hr prior to the test and assuring the patient had not taken antibiotics or bismuth salts for at least 4 wk prior to the test. In the nuclear medicine department the patient swallowed the capsule with

For reprints or correspondence contact: James H. Corley, RPh, MS, BCNP, Medical College of Georgia, Augusta, GA 30912-3950.

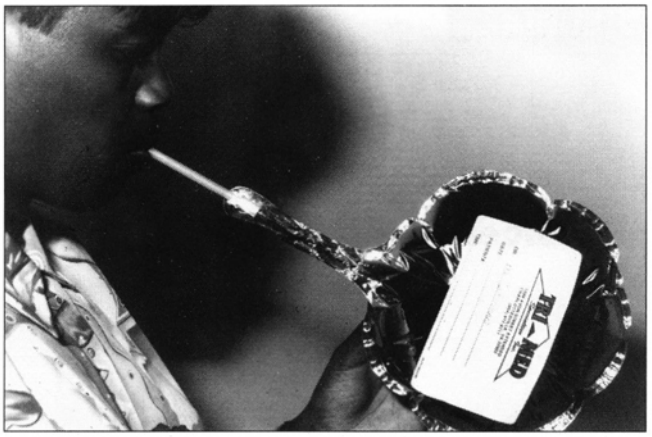

FIGURE 1. Demonstration of the technique used to collect a patient's breath sample.

30 ml of warm water to help the capsule dissolve in the stomach and release ^{14}C urea.

Three samples were obtained at 10, 15 and 20 min after the capsule was swallowed. Breath samples were obtained by exhaling through a straw into a 1.5-liter aluminized balloon (Fig. 1). The balloons were mailed by priority mail from the nuclear medicine department to Tri-Med Specialties, Inc. in Charlottesville, Virginia for testing (Fig 2).

Breath samples were considered negative if they contained <30 dpm, indeterminate if between 31–99 dpm, and positive if >100 dpm. These values were established by the manufacturer from a pilot study which had a <5% false positive rate. Raju, et al. reported the ^{14}C urea breath test had a high diagnostic accuracy with a sensitivity of 98% and specificity of 97% (*4*).

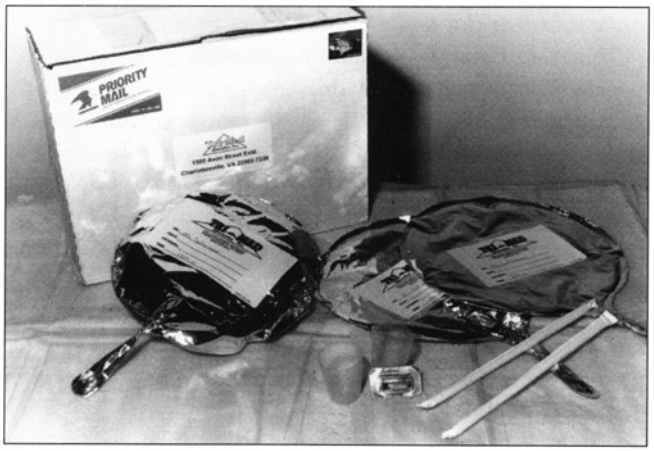

FIGURE 2. Carbon-14 urea breath test components from left to right: mailing box, inflated breath sample balloon, medicine cups, ^{14}C urea capsule (1 μCi), two unused breath sample balloons and two straws.

At the Medical College of Georgia, 31 patients undergoing upper gastrointestinal endoscopy for evaluation of peptic ulcer disease were studied using the ^{14}C urea breath test. Twenty-seven patients had a positive breath test, H. pylori seen on Giemsa stain and either gastric or duodenal ulcer. Four patients had a negative ^{14}C urea breath test, absence of H. pylori on Giemsa stain and no ulceration.

DISCUSSION

Carbon-14 is a naturally occurring isotope which is continuously formed in the earth's atmosphere. The dose from 1 μCi administered as ^{14}C urea equals the whole-body dose received from natural sources in an 11-hr period (0.3 mrem) (*5*). This low radiation dose should not prevent the wide use of the test, but may limit its usefulness in children and pregnant women.

Symptomatic patients with H. pylori infection require treatment with antimicrobial agents in addition to antisecretory drugs. H. pylori is sensitive to several antibiotics in vitro including amoxicillin, tetracycline and clarithromycin. The treatment's triple-drug regimen consists of bismuth subsalicylate in combination with two antimicrobial drugs, metronidazole and tetracycline or amoxicillin, because single antimicrobial agents are largely ineffective (*6*). Treatment of peptic ulcer is directed toward the eradication of H. pylori which can be monitored with a repeat ^{14}C urea breath test.

Recent discoveries concerning the role of H. pylori in peptic ulcer disease have changed the medical approach to ulcer diagnosis and therapy. A new noninvasive method using ^{14}C urea appears to be useful for diagnosis and evaluation of treatment in patients with peptic ulcer disease. This radiopharmaceutical may be available soon for use in the US and Canada.

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