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M.M. Karimov

*Republican specialized scientific and practical medical center of therapy and medical rehabilitation, Tashkent, 100094, Uzbekistan, mirvasit61@rambler.ru*

P.S. Zufarov

*Tashkent Medical Academy, Tashkent, 100109, Uzbekistan, pulatzufarov@gmail.com*

G.N. Sobirova

*Republican specialized scientific and practical medical center of therapy and medical rehabilitation, Tashkent, 100094, Uzbekistan, guzals@mail.ru*

S.T. Rustamova

*Republican specialized scientific and practical medical center of therapy and medical rehabilitation, Tashkent, 100094, Uzbekistan*

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## Employment of Respiratory $C_{14}$ Test with Helicobacter-Associated Diseases

Karimov M.M.<sup>a</sup>, Zufarov P.S.<sup>b</sup>, Sobirova G.N.<sup>a</sup>, Rustamova S.T.<sup>a</sup>, Karimova D.K.<sup>a</sup>

<sup>a</sup> SI "Republican Specialized Scientific Practical Medical Center of Therapy and Medical Rehabilitation"

<sup>b</sup> Tashkent Medical Academy

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### ABSTRACT

*The results of comparative assessment of the diagnostic value of the respiratory urease test labeled with  $C_{14}$  for the diagnosis of Helicobacter pylori infection in patients peptic ulcer and chronic gastritis B compared with serological test and rapid urease test on biopsies from the gastric mucosa were presented in the article. The results of study revealed that the sensitivity of the method was almost the same (95%) compared to biopsy rapid urease test. It was shown that presents of available licensed equipment and simplicity creates opportunity to use this method in specialized centers and regional multidisciplinary medical institutions.*

The global issue of modern gastroenterology is to solve the problem of diagnosis, treatment and prevention of complications of Helicobacter-associated diseases of the digestive system [3]. Currently, there is unambiguous scientific evidence of the connection Helicobacter Pylori (HP) infection with chronic gastritis, gastric ulcer and duodenal ulcer, malignant tumors of the stomach-adenocarcinoma and extra nodal B-cell lymphoma, which puts the diagnosis of HP infection and the choice of optimal treatment regimens for this infection in a number of the most important tasks of modern medicine [1, 2]. The Maastricht Consensus V directly indicate: Statement 1: H. pylori are the most important risk factor for stomach cancer. Eradication is the most promising strategy for reducing the incidence of gastric cancer (Level of evidence: 1, Recommendations class: A) [9]. The great interest of practical doctors in HP infection stimulated the creation of many different methods of its diagnosis. These include both invasive methods for determining HP infection by histological, urease tests, and representing a large and promising interest is a non-invasive breath tests. In the same consensus as the "gold standard" for the control of eradication recommends respiratory urease test with  $C_{13}$  labeled carbon. For all its informativeness, this technique has one limitation. This is the high cost of the equipment, which seriously limits its use in practical health care. An alternative to this technique is a carbon  $C_{14}$  labeled breath test.  $C_{14}$  is a radioactive isotope that is a source of low-energy beta particles. Its use had a number of restrictions and was subject to strict control, so this option was less common. The main problem with the use of urease breath test (UBT  $C_{14}$ - test) was the difficulty organization of work on the storage and transportation of radioactive drugs. In recent years, due to inroads into a new tech, equipment using small doses of carbon labeled  $C_{14}$  has been created and the above

sanitary standards have been cancelled. The application of microcapsules for packaging urea labeled with a radioactive isotope has minimized the difficulties associated with the storage, disposal and safety of this isotope. For example, in a number of countries, including China, India and European countries, the application of this technique does not require radioactive control [8]. In the US, the sale of microcapsules with urea labeled with carbon isotopes is allowed by the FDA on along with conventional medicines through the pharmacy network. In addition, the cost of equipment and consumable material at cost is quite acceptable for the budget of practical health care. Currently, this equipment and medicinal substance of carbon C<sub>14</sub> are registered in the Pharmacological Committee of the Republic of Uzbekistan.

**Objective:** Comparative evaluation of the sensitivity and specificity of the respiratory Urease test in patients with HP-associated diseases of the upper gastrointestinal tract (peptic ulcer and chronic gastritis B) compared with rapid urease and serological test for HP.

**Materials and methods.** Studies were conducted in 40 patients (22 men and 18 women, average age 45.5±3.6 years) with HP-associated diseases of the upper gastrointestinal tract (28 HP-associated chronic gastritis type B and 12 duodenal ulcer). Diagnosis verification was performed by esophagogastroduodenoscopy (EFGDS) with targeted biopsy and rapid urease test (ASAN Helicobacter Test, Republic of Korea) (Fig. 1).



**Figure 1.** The device for carrying a respiratory C<sub>14</sub> urease test

Also, these patients were assessed for HP infection by non-invasive respiratory urease test. A scintillation counter (HUBT-20PHelicobacterpyloridetector) was used to register the presence of C<sub>14</sub> in the exhaled air. As a control, all patients also were determined of HP by serological method in blood serum. Patients were defined eradication therapy according to the recommendations of the Maastricht Consensus V, including Proton Pump Inhibitor, Amoxicillin, Clarithromycin and Bismuth Tricalium Dicitrate (De Nol) for 14 days. Control of the effectiveness of eradication therapy was carried out 4 weeks after the end of therapy. The control study included the determination

of HP by a rapid urease test and a respiratory Urease test. The digital material is processed by the method of variational statistics.

**The results of the study and their discussion:** Studies conducted to assess the contamination of the gastric mucosa of patients with HP-associated chronic gastritis, showed that none of the using methods did not have 100% diagnostic information (Table. 1). The sensitivity of the rapid urease test conducted on biopsy material was 97.5%. Similar results were obtained in a breath test with C<sub>14</sub> carbon isotope. The sensitivity of the conducting technique during the serological study by enzyme immunoassay of blood serum was 95%.

**Table 1**

**Indicators of gastric mucosa contamination in patients with chronic gastritis by various diagnostic methods**

Method of diagnosis of HP	Before treatment, (HP+)		After treatment (HP+)	
	Number	%	Number	%
Rapid urease test	39	97,5	4	10%
Respiratory C <sub>14</sub> test	39	97,5%	4	10%
Serologicalmethod	38	95%	36	90%

Conducted studies have revealed that the results of the rapid urease test and the respiratory C<sub>14</sub> test were the same, where the effectiveness of eradication therapy was 90%. Serological method of detection of antibodies to HP, as expected, did not have such information.

As is well known, all existing methods of diagnosis of HP infection can be divided into direct and indirect. Direct methods can directly identify HP; indirect methods do not register the HP infection, but the consequences of its persistence in the body. As a method of primary diagnosis in persons who have indications for EFGDS, according to the Maastricht Protocols, it is recommended to use a rapid urease test from a biopsy selected by the antrum and the body of the stomach (Level of Evidence: 4 and Recommendations Class: C) [10].

HP in the process of its life activity produces the enzyme urease, which accumulates in the gastric mucosa. Urease decomposes urea to carbon dioxide and ammonium ions. To identify urease, the presence of which indicates the presence of HP, various biochemical techniques have been proposed. In diagnostic environments, necessarily including urea and indicator was placed biopsy material. If the environments begin to accumulate ammonium-the product of hydrolysis of urea urease, its pH changes and the indicator changes color. Urease test is simple to perform, does not require special qualification of medical personnel, relatively inexpensive, allows you to quickly get the response (depending on the modification of the test, the result can be obtained in a few minutes, at most after 24 hours) [6].

Despite the simplicity and availability of the biochemical method for detecting HP in biopsies of the gastric mucosa, it has a number of significant downsides. Urease tests give information of the presence of HP only in one area of the gastric mucosa; biopsies are not suitable for subsequent histological examination. These restrictions do not allow carrying out a clear correlation between its structural changes and urease activity in the same part of the gastric mucosa.

The significant disadvantages include the possibility of obtaining false positive results, as it is shown that in patients with pathology of the gastrointestinal tract, its upper parts are populated by gram-negative bacteria, of which many species are able to produce

urease, and the most common in humans *Proteus vulgaris* and *Proteus mirabilis* are able to decomposed urea in the same time as HP [11]. In addition, the technique is invasive and the key positions of the Maastricht Consensus indicate: a suitable treatment strategy “Test and Strategy” the use of non-invasive methods of diagnosis and subsequent treatment in case of positive results [10].

Radionuclide methods of infection diagnostics (noninvasive and indirect) are based on urease activity of HP - urease respiratory tests with urea labeled with isotopes  $C_{13}$  and  $C_{14}$  [7]. In 1987, D. Graham et al. [5] published data on the first method labeled with  $C_{13}$  urea, *Campylobacter pylori* in the gastric mucosa. Labeled urea is given to the patient as part of a trial breakfast. HP urease decomposes urea to carbon dioxide, preserving the labeled carbon.

Carbon dioxide with blood flow is delivered to the lungs and excreted with exhaled air. The patient exhales into a special tube-container, and the air sample is sent for analysis. A scintillation counter is used to register the presence of  $C_{14}$  in the exhaled air. Since the respiratory test does not require esophagogastrosocopy, this method is applicable in patients to whom it is contraindicated. This test gives information of all gastric mucosa and not a single fragment of it. Its sensitivity reaches 99% and specificity-98%. The high cost of the mass spectrometer limits the implementation of a breathing test using the isotope  $C_{13}$  [4].

As mentioned above, the emergence of new, innovative technologies have made it possible to conduct a test with the labeled isotope  $C_{14}$  without fear of its radioactive properties. The creation of new scintillation counters allowed the use of the drug  $C_{14}$  in extremely low dosages. As shown by our studies this technique has the same high (95%) sensitivity both in the primary diagnosis and in the control of eradication of HP infection. The availability of a licensed scintillation counter and  $C_{14}$  preparations, which differ from the traditional  $C_{13}$  breath test at an affordable cost, creates an almost real possibility of widespread use of this method of HP diagnosis at the level of practical health care.

### Summary:

1. Respiratory urease test with  $C_{14}$  isotope has almost the same sensitivity (95%) compared to biopsy rapid urease test in the diagnosis of HP infection in patients with HP-associated diseases of the digestive system.

2. During control the eradication of HP infection from the gastric mucosa of patients with HP-associated gastrointestinal diseases, preference should be given to non-invasive diagnosis using a respiratory  $C_{14}$  test.

3. The availability of licensed equipment and consumables at affordable prices compared to the  $C_{13}$  test, the simplicity of the tests creates a real opportunity to use this technique in the conditions of both specialized centers and at the level of regional multidisciplinary medical institutions in accordance with clinical protocols for the diagnosis and treatment of diseases of the digestive system.

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