VIA MEDICA
Vol. 4, No. 2, pp. 101–103

ISSN 1506–9680
communi-cations

^{14}C-urea breath test in the detection of Helicobacter pylori infection

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Abstract

Helicobacter pylori infection is supposed to be one of the major causes of digestive and other diseases. Among a lot of invasive and non-invasive methods for its detection, none is ideal. The aim is an assessment of the Helicobacter pylori infection in the stomach using breath test and comparison to other diagnostic methods, as well as following up the effects of therapy.

In 17 patients with digestive discomfort, breath test, rapid urease test and histology were performed, while in 47 patients with proven HP infection the effect of therapy was followed up using breath test and clinical findings. Breath test was performed after per oral administration of the capsule of ^{14}C urea (37 kBq). Findings of the breath and urease tests were in accordance in 14/17 patients (83%) while breath test and histology in 16/17 patients (94%). During follow-up of the therapeutic effects, breath test and clinical findings were in accordance in 43/47 patients (98%).

Breath test can be useful in diagnosis but is a method of choice in following up the patients after therapy for H. pylori infection, because it is non-invasive, fast and precise.

Key words: Helicobacter pylori, breath test, ^{14}C-urea

Introduction

Helicobacter pylori (HP) is probably the most common bacterial pathogen with an incidence of up to 50% in some parts of the world. Occurrence of the disease attributed to the presence of this bacterium depends on the infection, as well as on the immune response and predisposition of the patient. Sequel can include chronic superficial gastritis, duodenal or gastric ulceration, gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma. Also, the presence of Helicobacter pylori can be connected with some non-digestive diseases (ischaemic heart disease, autoimmune diseases, late puberty, delayed growing-up etc.) [1].

H. pylori has a unique way of adapting in the stomach environment. It goes through the mucous layer to infect gastric epithelial cells, and produces enzymes that break down substances in gastric juice. The most important of these enzymes is urease. Urease converts urea from saliva and gastric juices into bicarbonate and ammonia, which are strong bases and thus protect bacteria from stomach acidity. The by-product-carbon dioxide-is absorbed into the circulation and exhaled. Urease is found in much higher concentrations in H. pylori than in any other bacteria, which enables performance of an accurate, sensitive, specific and non-invasive diagnostic test. Thus, when an infected patient swallows a dose of urea labelled with an isotope ^{14}C Helicobacter pylori in the gastric mucosa break down the labelled urea to form ammonia and labelled carbon dioxide, which is being absorbed and exhaled. After the collection of a certain amount of $^{14}CO_2$, beta counter measures the radioactivity.

^{14}C is a low energy beta-emitter (49 keV_{mean}, 156 keV_{max}) with maximal range in water of 0.3 mm and physical half-life of 5730 years. $^{14}CO_2$ reaches the maximal activity in the exhaled air after 10–15 min, decreasing during time with biological half life of $T_{½}$ = 15 min. ^{14}C urea which was not broken up is excreted by urine with $T_{½}$ = 12 h, while 10% of ^{14}C remains in the body after 72h and is excreted with $T_{½}$ = 40 dana [2]. ^{14}C-urea that is not broken up by bacteria is eliminated by urine.

The aim of this study is detection of the presence of Helicobacter pylori, correlation of the results with other methods (fast urease test, pathohistology), as well as monitoring of the therapy response in the infected patients by breath test and clinical findings.

Material and methods

We investigated two groups of patients. In the first one, consisting of 17 patients with digestive discomfort, breath test, rapid urease test and histology were performed, and findings correlated. In the other group, consisting of 47 patients with proven

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infection with Helicobacter pylori, the effect of therapy was followed up using breath test and clinical findings. Initial therapy consisted of a combination of two antibiotics (metronidazol, clarithromycin, amoxycillin) plus proton pump inhibitors, during seven days. If the infection persisted after a month following the end of the therapy, the combination of antibiotics (azytromycin) was changed, and used with colloid bismuth, proton pump inhibitors or H2 antagonists.

Four biopsy samples were taken from the antral mucosa for pathohistology and fast urease test. Radionuclide breath test was performed using commercial kit (capsules and vials containing trapping solution-Helizo, Izotop, Hungary). It was done before (background value estimation) and 30 minutes after per oral administration of the capsule containing ^{14}C urea (37 kBq). The patients exhaled in the KOH solution (with timolphtalein) until it became colourless, which was the sign that a certain amount (1 mmol) of CO_2 had been trapped. After adding the 15 ml of scintillation fluid (Ecolite ICN-Biomedicals), radioactivity in the collected samples before and after ingestion of the capsule was measured by (LKB Wallac — Rack Beta Spectral) liquid scintillation counter, during 5 minutes.

Results

According to our results, the rise of activity over 100% was considered positive. From 17 patients, 7 were breath test positive, 9 negative and one equivocal. Fast urease test was positive in 6, negative in 11, while histology was positive in 7 and negative in 10 (Table 1). Findings of the breath and urease tests were in accordance in 14/17 patients (83%) while breath test and histology in 16/17 patients (94%).

During follow-up of the therapeutic effects, breath test and clinical findings were in accordance in 43/47 patients (98%).

Discussion

Our results point out that the rise of activity over 100% in comparison to the background may be considered as a positive finding, and that the results correlate with the ones obtained by other methods. Also, we confirmed the value of the method in the follow-up of the effects of therapy, thus excluding the need for the use of invasive methods.

Our results are in accordance with the results of other authors. So, Kaul [3] obtained very significant rise of the radioactivity in the collected samples in Helicobacter positive persons ($p < 0.001$). Jensen [4] proved that sensitivity and specificity of the method are 100% in comparison to the fast urease test, while in comparison to pathohistology 100% and 89% respectively. The results of other authors point out [5–9] that sensitivity and specificity of these investigations were 90–98% and 87–100% in comparison with histology and the culture of biopsy specimen.

Table 1. Comparative findings of the different methods in the detection of Helicobacter pylori infection

METHOD	FINDING (+)	FINDING (–)	FINDING (+/-)
Breath test	7	9	1
Fast urease test	6	11	
Pathohistology	7	10	

^{14}C-urea breath test is both sensitive and specific for H. pylori; it detects only urease-producing organisms and reflects total gastric urease activity, and results are reproducible. It tells whether a patient is actively infected, and it can be used for follow-up the treatment. However, it is necessary to perform the investigation at least 4 weeks after the end of the antibiotic therapy and two weeks after the therapy with sucralfates or proton pump inhibitors in order to avoid false negative finding [10]. Also, caution is needed in the interpretation of the findings in the patients with gastric resection, which can be false negative because of the fast elimination of the capsule or false positive because of achlorhydria or colonisation with Helicobacter-like bacteria, which can also break up urea. The investigation must be done at least 6 hours after the last meal. Some authors conclude that the radiation dose absorbed by a patient can be compared to the one received from natural radiation sources during one day [5, 11, 12], while the most pessimistic criteria claim [4] that the dose absorbed in this way can be compared to the one absorbed during radiography of the teeth (up to 20 μSv). Caution is necessary in implementation of the method in pregnant and nursing women but it can [2] be performed without risk in children.

Besides ^{14}C-urea breath test, non-invasive methods for the detection of Helicobacter pylori are ^{13}C-urea breath test as well as serologic analysis. The ^{13}C isotope is not radioactive and so is safer, although expensive instruments, which are not widely available, are required to detect it. Serologic tests can tell only if infection has occurred within the past year, not whether the patient is currently infected. Endoscopy and biopsy require unpleasant medical procedures, and laboratory analysis. They can detect current infection only if they hit an area in which the mucosa is infected, because of its patchy distribution. Besides, this method carries a certain risk of re-infection with Helicobacter pylori from the oral cavity.

^{14}C-urea breath test can be used in diagnosis, but is a method of choice in following up the effect of therapy in patients with Helicobacter pylori infection, because it is non-invasive, rapid, sensitive, specific and available.

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