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Research Article

Features of *Helicobacter pylori* Infection in Patients with Diffuse and Intestinal Gastric Cancer According to a Urease Test, Operated Under the Conditions of "Multidisciplinary Medical Center" of Nur-Sultan

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Abstract

Helicobacter pylori was discovered by Australian scientists B. J. Marshall and J. R. Warren in 1983, which caused incredible progress in gastroenterology [1]. In scientific studies, as well as in 1994, the International Agency for Research on Cancer attributed helicobacter infection to carcinogens of the first order [2,3]. The Lauren classification, proposed back in the 60s, divided gastric adenocarcinoma into two main histological types: 1-well-differentiated or intestinal type, and 2-undifferentiated or diffuse type [4]. According to literature sources [5], diffuse gastric cancer arises from the normal gastric mucosa without any precancerous stage and is often not associated with *Helicobacter pylori*. Others [6] also indicate that when 1246 patients with various *Helicobacter pylori*-associated gastroduodenal diseases were observed for 8 years, stomach cancer was detected in 36 (2.9%) of them, including 23 cases with intestinal and 13 with its diffuse form. According to [7], the infection rate of patients with stomach cancer in the Orenburg region of Russia with various histological forms of stomach cancer is 85.7% of cases with G2 gastric adenocarcinomas, in 61% of cases of ring-cell cancer, in 50% of cases of G3 and G4 gastric cancer, in 45% of cases of highly differentiated gastric adenocarcinomas and in 70% of cases with other histological forms of stomach cancer. In our study, we tried to clarify the situation of the relationship of diffuse stomach cancer with *Helicobacter pylori* infection in patients operated in the MMC of Nur-Sultan.

Keywords: Diffuse Gastric Cancer; Intestinal Gastric Cancer; *Helicobacter pylori*; Infection

Introduction

The production of *H. pylori* of a large amount of the urease enzyme has led to the creation of methods for its indirect detection in the human body. One such method is the rapid urease test. The first rapid urease test CLO test (Delta West Ltd., Bentley, Australia) was developed by Marshall B.J., Warren J.R., *et al*. [8] for the detection of *H. pylori* in the gastric mucosa. After that, this method began to be widely used in clinical practice. Currently fast urease the test, together with the morphological method, is the most commonly used invasive method for diagnosing *H. pylori* infection in the stomach [9]. According to the recommendations of the 3rd and 4th Maastricht Consensus 2005 and 2012 on the diagnosis and treatment of *H. pylori* infection, when a patient undergoes video esophagogastroduodenoscopy, it is recommended to use a rapid urease test to diagnose a microorganism [10-12].

The test is based on the detection of the urease enzyme by a biochemical method [13]. The production of *Helicobacter pylori*

urease leads to its accumulation in the stomach tissue [14]. This makes it possible to use methods for detecting urease directly in mucosal biopsies. To date, many different tests have been proposed to detect urease in the gastric mucosa. All biochemical tests are based on the same principle. During the hydrolysis of urea under the action of urease, the resulting ammonium ion leads to a strong increase in the pH of the medium. This is fixed with an indicator (in most cases phenol red is used), as well as visually, by changing the color of the medium (phenol red is yellow at pH 6.8, and bright crimson at pH 8.4) [14]. By changing the color of the reagent, the urease activity of the biopsy is determined [8].

Most rapid urease tests are aqueous urea with an indicator. The identification effect appears after the biochemical reaction of the decomposition of urea by the enzyme Hp urease, which is in the biopsy. In this case, the assessment is carried out within 24 hours of incubation. These are the so-called "cold" methods that work at room temperature and contain bactericidal additives that destroy any microflora in the biopsy. The main disadvantage of these tests is instability during long-term storage (discoloration of the solution), diagnostic time (24 hours) and the inability to use the biopsy for further histological or bacteriological examination, as a result of the color of the latter with an indicator and a violation of its morphological structure. The membrane array promises a new diagnostic tool to detect *H. pylori* more sensitively than the CLO test. These results suggest that urease may play an important role in the development of hyperproliferation of the gastric mucosa in *H. pylori*-induced gastritis [15].

All these shortcomings are absent in new generation urease rapid tests, one of which is the HELPIL test system (HELPIL® test system (release forms: Tape, AMA LLC, Russia according to the standard method). The HELPIL rapid urease test uses a more efficient indicator system and a special fibrous carrier. This made it possible to perform the test in the form of test tickets in individual packaging and not to use an aqueous solution. Test tickets can be stored at room temperature for a long time. The indication effect of the HELPIL test system appears directly during the biochemical reaction of urea decomposition by the enzyme Hp urease, at the end of the reaction, the staining intensity weakens and disappears, therefore, the reaction is evaluated in the first 3 minutes of placing the biopsy sample for the test, without 24-hour incubation. It should be noted that only for the HELPIL form there is an additional possibility of reading the result from the reverse side. The paper in the test tickets has capillary sorption properties, absorbs liquid from the biopsy, does not stain it and does not damage the structure of the latter. Therefore, the biopsy can be used for further histological examination.

Thus, the aim of the study was to evaluate the clinical efficacy of using the HELPIL rapid urease test for the diagnosis of *H. pylori* (Hp) in the antrum, cardiac sections and the body of the stomach along a small curvature.

Materials and Methods

A test for the determination of urease activity was conducted in 31 patients diagnosed with stomach cancer in the "Multidisciplinary medical Center" Nur-Sultan for the period from 28.04.20 to 07.04.21. Infection of the gastric mucosa was detected in 24 patients (77.41%). The test for the determination of urease activity was carried out on biopsies of 2-3 mm in size taken from the gastric mucosa in the antrum, cardiac sections and the body of the stomach along a small curvature (Figure 1) using a device for rapid diagnosis of the presence of Helicobacte pylori by the urease activity of the biopsy (*in vitro*), (HELPIL® test system (release forms: Tape), AMA LLC, Russia according to the standard method). The statistical parameters were calculated in the R program.

Figure 1: Diagram of the sites for taking a biopsy of the gastric mucosa.

As sources of mucosal biopsies, macro preparations of stomachs were used (within 2-3 hours after surgery, Figure 2), patients operated under the conditions of "Multidisciplinary medical Center" Nur-Sultan.

Figure 2: Postoperative material of the stomach of a patient operated in "Multidisciplinary medical Center" Nur-Sultan.

Conducting a test to determine urease activity.

- I remove the tab from the indicator disk.
- I take a biopsy sample from the gastric mucosa in the antrum, stomach body, cardiac department along a small curvature (Figure 3).
- I place the biopsies obtained during the sampling of the gastric mucosa on the surface of the indicator disk.
- I register the appearance of a green/blue spot within three minutes in the photo report (Figure 4).

Figure 3: Sampling of a biopsy of the gastric mucosa by a small curvature in the cardiac compartment of the stomach.

Figure 4: Application of a biopsy of the antral part of the gastric mucosa to the indicator disk of the HELIL tape. Registration of coloring in the photo report.

Results

In our study, in patients diagnosed with diffuse gastric cancer, the presence of urease activity of *Helicobacter pylori* in the gastric mucosa was detected in 83% (15 cases out of 18) of patients. It should be noted that negative results of tests for urease activity were not observed at all in patients diagnosed with diffuse gastric cancer (G3, G4, ring-shaped cell c-r) under 40 years of age. Three cases of negative results in diffuse cancer were noted in patients aged 70, 55, 72 years. Patients with gastric cancer with a degree of differentiation of G1 and G2 younger than 40 years were not represented in the study due to their absence during the study period. In intestinal gastric cancer, the infection of the gastric mucosa was 69 % (9 patients out of 13). There is also a more frequent infection of 3 parts of the stomach (cardia, stomach body, antral section with a small curvature) with a diffuse form of stomach cancer than with an intestinal one-77.77% (14 cases out of 18 are diffuse), against 4 cases out of 13 with (30.77%).

Discussion

As a result of the conducted work, the features of infection with *Helicobacter pylori* of the gastric mucosa were revealed. It is noted that almost all patients diagnosed with diffuse stomach cancer under the age of 40 are infected. In addition to the above, there is an infection of three parts of the stomach along a small curvature, whereas with intestinal cancer, the antral part is more often infected. There are cases when an infection with intestinal stomach cancer occurs in three departments, but less often. It is also worth noting that patients with a diagnosis of intestinal stomach cancer under 40 years of age were not represented in the study, since such patients did not occur during the study period.

The above-mentioned features of infection may be associated with a younger age of patients, since infection occurs at a younger age (in childhood, adolescence) and there is a change in the acute phase, the chronic phase of anacid atrophic gastritis associated with Hp infection with a transition to the phase of atrophy, metaplasia with subsequent malignancy. Thus, with diffuse stomach cancer, we are faced with an earlier and active phase of infection, and with intestinal with a later and less "bright" one. But it is impossible to exclude the peculiarities of immunity in this category of patients, namely suppression, which allows the infection to manifest itself more actively and colonize a large number of stomach sections and there is a higher probability of a malignant neoplasm at a young age (under 40 years) against the background of a decrease in immunity. Thus, it is necessary to increase the number of studied objects to confirm the conclusions of this work, and if this theory is confirmed, there are opportunities and prospects for research in finding the cause of this pattern: immunosuppression or the natural process of changing phases, stages of interaction between infection and the gastric mucosa.

Conclusions

According to the correlation analysis, closely significant results were obtained that allow us to conclude that with diffuse RV with age, helicobacter infection and its number in the stomach departments are less (p-value = 0.08971; cor = -0.39) and (p-value = 0.06731; cor = -0.42). In intestinal cancer, there is no significant dependence on helicobacter infection, and the number of infected HP increases with age (p-value = 0.0657; cor = 0.57). These conclusions serve as a hypothesis that can be solved by increasing the power of the study (sample).

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