

PRACA ORYGINALNA  
ORIGINAL ARTICLE

## THE EFFECT OF INTRACELLULAR “DEPOT” *HELICOBACTER PYLORI* INFECTION ON THE QUALITY OF ERADICATION WITH MONOTHERAPY OF PATIENTS WITH CHRONIC NON-ATROPHIC GASTRITIS BY THE BISMUTH COLLOIDAL SUBCITRATE

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### ABSTRACT

**Introduction:** Noted that monotherapy by the bismuth colloidal subcitrate in the treatment of chronic HP- infection is effective only in 14-40% of cases, but all the reasons that reduce its effectiveness, are not fully explored.

**The aim:** To determine the effectiveness of monotherapy by the bismuth colloidal subcitrate among patients with chronic non-atrophic gastritis with or without intracellular “Depot” of HP- infection.

**Materials and methods:** The 36 patients took comprehensive examination: step-by-step pH-metry, esophagogastroduodenoscopy, *helicobacter* infection test (HP) (*helicobacter* urease test and microscopic examination of stained smears), histological investigations of the gastric stump mucous, stool test, HELIC – test, the level of natural killers (CD-16). Control studies were performed 1 months after 1-month monotherapy by the bismuth colloidal subcitrate and included a stool test and HELIK- test.

**Results:** *Helicobacter* infection was detected in 100% of cases. When using two methods: comparing the results of urease test and smears, prints, and the level of natural killer CD-16 intracellular “depot” HP was detected in 29 (80.6%) patients. While control research in 1 month it was found that monotherapy was effective only among 7 (19.4%) patients whose primary integrated survey did not reveal intracellular “Depot” HP- infection.

**Conclusions:** The bismuth colloidal subcitrate is not effective in the presence of intracellular “depot” HP. The definition of “depot” should be carried out by two methods: comparing the results of urease test and smears- prints, and the level of natural killers (CD-16).

**KEY WORDS:** chronic non-atrophic gastritis, intracellular “Depot”, bismuth colloidal subcitrate

Wiad Lek 2019, 72, 10, 1909-1911

### INTRODUCTION

Discovery of *Helicobacter pylori* (HP) in the year 1983 by Australian scientists B. Marshall and J. R. Warren has become a new landmark in understanding the etiology of such diseases as chronic gastritis type B (chronic non-atrophic gastritis), peptic ulcer disease, stomach cancer and MALT-lymphoma [1]. Regarding this the views on the form the data treatment of pathologies began to form that caused the creation in 1993 year the 1-st Maastricht consensus which defines the schema of the treatment of chronic *Helicobacter pylori* infection. Further consensus was reconsidered now only once and now exist the 5-th Maastricht consensus, which was adopted in the year 2015 (Florence). This consensus noted the effectiveness of quadra therapy, which, in addition to Proton pump inhibitors and their two antibiotics, includes drug of bismuth - bismuth colloidal subcitrate [2, 3, 4, 5, 6, 7, 8, 9, 10, 11]. Noted that monotherapy by the bismuth colloidal subcitrate in the treatment of chronic HP- infection is effective only in 14-40% of cases [5], but all the reasons that reduce its effectiveness have not been fully studied, including the ability of HP infection to penetrate into the parietal cell and form intracellular “depot” under the influence of prolonged stress and the use of proton pump inhibitors [12].

### THE AIM

To determine the effectiveness of monotherapy by the bismuth colloidal subcitrate among patients with chronic non-atrophic gastritis with or without intracellular “Depot” of HP- infection.

### MATERIALS AND METHODS

In the period from January 2016 till January 2017 on the basis of the clinical division of the problem lab on chronic *Helicobacter pylori* infection of the Petro Mohyla Black Sea National University was initially examined and treated in an integrated manner with the subsequent quality control of eradication 36 patients with chronic non-atrophic gastritis. The age of patients ranged from 23 to 51 year (the meddle age was  $30.6 \pm 1.27$  y.); males was 21 (58.3%), female-15 (41.7%).

Primary comprehensive survey included: step-by-step intra-gastric pH-Metry based on methodology by Chernobrovii V.N esophagogastroduodenoscopy(EGDS) by generally accepted method, double HP testing: test for ureaz activity and microscoping stained by Giemsa smears, material for which was taken during endoscopy from 4 topographical zones: from the middle third of the gastric antrum and body of stomach on the big and small curvature with our created methodology, which

**Table I.** Degree of semination of gastric mucosa with HP infection on topographical zones of patients with chronic non-atrophic gastritis while primary survey

Topographic zones of the stomach	Degree of semination of gastric mucosa with HP infection on zones ( + ) / ( M ± m )
Antral section	a) 2,13 ± 0,28; b) 2,16 ± 0,28
Body of stomach	a) 2,14 ± 0,28; b) 2,45 ± 0,28

Note: n-the number of studies: a) large curvature, b) small curvature.

**Table II.** Results of stool-test and HELIK-test before and after treatment among patients with chronic non-atrophic gastritis

Name of the test	Positive result of test			
	Before treatment		After treatment	
	Amount of tests	%	Amount of tests	%
Stool-test	36	100	29	80,6
Helik-test	36	100	29	80,6

allows to define both the presence of intracellular “Depot” HP infection and also histological studies of the gastric mucosa, the material for which is taken from the same zone, using a generally accepted method taking into account recent classification [13, 14]. In addition, all the patients additionally was made the stool test in our test modification [15] and HELIK-test in our test modification [16], as well as determined the presence of intracellular “Depot” of HP infection on the level of natural killers (CD-16) [17]. Control studies were performed 1 months after the end of monotherapy by the bismuth colloidal subcitrate, which lasted 1 month, and included a stool test and HELIK test.

The study was conducted in accordance with the basic bioethical provisions of the Helsinki Declaration of the World Medical Association on the ethical principles of scientific 549 medical research involving human (2013) and the order of the Ministry of Health of Ukraine No. 690 dated September 23, 2009, which was confirmed by the findings of the meeting of the Ethical Commission of Petro Mohyla Black Sea National University, Nikolaev No. 3 dated March 12, 2019.

Primary sequence survey: first patients conducted pH-metry and then EGDS with biopsy material for testing in HP and histological studies of the stomach mucosa. The study was conducted in the morning on an empty stomach, in 12-14 hours after the last meal. The data obtained were processed statistically using Student t-test with the computation of averages (m) and perhaps the likelihood of deviations (m). The changes were considered to be statistically significant at  $p < 0.05$ . Statistical calculations were performed using Excel tables for Microsoft Office.

## RESULTS AND DISCUSSION

When carrying out the pH measuring all acidity levels have been identified, except hyperacidity and anacidity: hyperacidity is moderate - 5 (13.9%), normacidity-15 (41.7%), moderate hyperacidity-10 (27.8%), distinct hyperacidity -6 (16.6%).

While conducting EGDS active Ulcerative process was not identified in the stomach and in duodenum, but 3 (8.3%) patients had manifestations of ulcers duodenal bulb in the past as scar deformity of varying degrees of severity. When analyzing data of histological investigations of all patients in 100% of cases have confirmed the existence of chronic non-atrophic gastritis in both active and inactive stages of varying degrees of severity.

When testing on HP *Helicobacter* infection was detected in 100% of cases when the degree for semination from ( + + ) to ( + + + ). Data on the extent of the gastric mucosa for semination of HP infection on topographical zones of the stomach patients with chronic non-atrophic gastritis are reflected in table I.

During comparative analysis of data on the medium degree of semination with HP infection on gastric mucosa topographical zones reliable differences were found ( $p > 0.05$ ).

While conducting comparative characteristics urease test and data according to microscoping of stained smears to determine the presence of bacteria in the stomach lining cells intracellular “Depot” HP-infections were found only in the body of the stomach mucosa of 19 (52.7%) patients: 7 (19.4%) only in the body of the stomach mucosa of large curvature 8 (22.2%) only in the body of the stomach mucosa on small curvature, 4 (11.1%) in the membrane of the body of the stomach and small and large curvature.

When defining the intracellular “Depot” of HP infection on the level of natural killers (CD-16) the presence of bacteria in the cells were confirmed in 100% of patients' cases in whom they have identified in the first methodology, as well as 10 (27.8%) patients have. The mean value of the absolute levels of natural killer cells in the blood of the surveyed totaled  $754 \pm 3.34$  cells/ $\mu$ l (with norm-70-552 cells/ $\mu$ l).

Data on primary survey before treatment and secondary survey after treatment with the help of a stool-test and HELIK-test are shown in table II.

During the analysis of obtained data, it was found that the negative were stool test and HELIK test after treatment had only 7 (19.4%) patients whose initial examination did not reveal intracellular “Depot” of HP infection by any of the methods.

These results are understandable from the point of view of impact characteristics of the bismuth colloidal subcitrate on HP infection. The bismuth colloidal subcitrate is a surface antiseptic and affects on all forms of *Helicobacter pylori* infection when it is on the surface of the gastric mucosa. Although there is evidence that the particles of the bismuth colloidal subcitrate are captured by the epithelium of the stomach mucosa [4, 5], the process apparently poorly expressed, therefore, in the presence of intracellular “Depot” HP infection needs to be the bismuth colloidal subcitrate combined with two antibiotics that penetrate deep into the stomach mucosa [18].

## CONCLUSIONS

1. The bismuth colloidal subcitrate is not effective in the presence of intracellular "depot" HP.
2. The definition of "depot" should be carried out by two methods: comparing the results of urease test and smears- prints, and the level of natural killers (CD-16).

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*The work is a fragment of research work «Development of information and communication technologies in the system of medical examinations of seamen», the state registration number 0109U008375.*

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### Conflict of interest:

*The Authors declare no conflict of interest.*

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**Received:** 25.04.2019

**Accepted:** 17.09.2019