

MEDICAL SCIENCES

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ELICITATION ANTIBODIES OF IgG TO HELICOBACTER PYLORI INFECTION AND THE FREQUENCY PREVALENCE AMONG PATIENTS MULTIPLE MYELOMA AND POTENTIAL DONORS OF HEMATOPOIETIC STEM CELLS

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Abstract

The article presents the results of studies using an invasive method for diagnosing the levels of antibodies IgG to H.pylori infection among patients multiple myeloma residents of Kirgizia in collation with donors of hematopoietic stem cells.

In patients with MM of the kirgiz nationality, negative in 39% of cases and less often low, medium, high levels of IgG antibodies to H. pylori infection are detected in comparison with patients with MM of the Russian-speaking population of Kirgizia. At comparative assessment of indicators of patients with MM of the kirgiz nationality elicitation negative levels antibodies of IgG to H. pylori infection in 20% of cases and in potential donors of hematopoietic stem cells in 80% of cases. Among patients MM of the Russian-speaking population of Kirgizia have elicitation negative levels antibodies of IgG to H.pylori infection in 63% of cases and low in 70% of cases by compared with healthy residents of the North-West region of the Russian Federation.

A study at for the first time elicitation patients MM definition on antibodies for IgG to H. pylori infection makes it possible to early diagnose H.pylori infection and recognize pathology of the gastrointestinal tract (atrophic, erosive, erosive- ulcerative gastritis, steroid ulcers, gastric and duodenal ulcers), where inevitable transfer of tableted steroid drugs on intravenous administration, as well as in parallel with basic targeted therapy, in combination antibiotic therapy with H2-blockers, proton pump inhibitors, antacids. In this connection according to indications, timely push aside patients with MM from bone marrow autotransplantation and dismissal potential donors from donation of haploidentical (brother, sister), closely related, unrelated hematopoietic stem cell transplantation. When remission is achieved, patients with MM should, according to indications, carry out standard eradication therapy in combination with bacterial strains.

Thus, in oncohematological diseases, these studies at the present stage, the detection of H. pylori infection with prophylactic purposes in donors of hematopoietic stem cells and in patients with MM is a serious step and a reliable platform for studying immunogenetic and population characteristics, and identifying clinical and laboratory markers, the presence of infectious complications while taking frequent, basic steroid drugs, during conduct targets and planned polychemotherapy.

With timely diagnostic, treatment at an early stage of the basis disease, the duration of remission will increase and the period of remission of the underlying disease, receiving standard modern eradication therapy will increase the life expectancy of patients with MM.

Keywords: morbidity, diagnosis, eradication therapy, prevention.

INTRODUCTION

Currently, infection Helicobacter pylori(H.pylori) worries everyone, occurs in developed and in developing countries, and detected in people of all races, as among adults population, so and among children.

At the development and prevalence of a whole series oncohematological diseases, a large value impart viruses and bacteria are of great importance. Elicitation of infection of the organism, in particular, by the carrier of H.pylori infection and among potential donors of hematopoietic stem cells living in different geographical areas[1], as well as at benign, malignant oncohematological diseases, is important for the development

of effective treatment and determining the prognosis of the disease.

Among malignant oncogematological diseases, according to the classification of the World Health Organization(WHO, 2001)[2], disease MM refers to peripheral B-cell lymphoid tumors, developing gradually, which indicates a low degree of its malignancy.

However, multiple myeloma is considered a disease of old age, but in last years observed a trend towards rejuvenation of the disease. Patients with MM occur in the population of 2-3 cases per 100 000 population per year [3].The morbidity in Europe constitute

6:100 000 populations per year [4]. At the treatment of the underlying disease, H.pylori infection plays large, an important role at the oncohematological diseases.

At the initial stage plays an important role the duration and depth of damage to the gastric mucous membrane, then the emergence of an inflammatory pathological process and its gradual transition to a chronic form (atrophic, erosive, erosive gastritis, gastric ulcer, duodenal ulcer, drug gastritis, steroid ulcers), as well as in the development of a malignant tumor process "carcinogen for humans" by a factor deeply involved in the genesis of cancer, gastric lymphoma MALT-type. Despite the timely diagnosis of MM and initiated targeted therapy, in durable reception courses of steroid, non-steroidal anti-inflammatory, chemotherapy medicines, that more often to lead in additionally to damage to the gastrointestinal tract.

To date, with timely diagnosis, modern, effective therapy regiments and basic drugs for the treatment of H. pylori infection have been proposed. According to the recommendations, the Maastricht Agreements (consensus Maastricht-II) are divided into mandatory and expedient[5], a quadrotherapy scheme is proposed,[6] and in consensus (Maastricht-III)[7] separate formulated provisions on the treatment of H.pylori infection have been added.

In this connection, the aim of our study is the early detection of levels antibodies of IgG to Helicobacter pylori infection and to determine the frequency of prevalence and degree defeats of the gastrointestinal tract in patients with multiple myeloma residents of the Kyrgyz Republic (Kirgizia).

MATERIALS AND METHODS STUDY:

From March 2014 to July 2022, the study group included 39 patients (25 men, 14 women), with different stages of the course and immunochemical variants disease of multiple myeloma (MM). Of these 11 patients of kirgiz nationality(4women, men-7) and the Russian-speaking population (mixed nation and different nationalities) residents of Kirgizia-28 patients (women-10, men-18), aged 38 to 80 years, all patients is are citizens of the Kyrgyz Republic (Kirgizia).

The study was conducted on the basis of the Eurasian center of oncohematology, immunology and therapy, in the laboratory of St. Petersburg NIIEM named after Pasteur, the National Center of Oncology and Hematology of the Kyrgyz Republic (Kirgizia), in the laboratories of polyclinics, clinics in city Nursultan Kazakhstan, city Bishkek Kyrgyz Republic(Kirgizia),.

The control group consisted of 79 healthy residents of the North-West region of the Russian Federation and 84 potential donors of hematopoietic stem cells of kirgiz nationality from the National Register of Hematopoietic Stem Cells of Kirgizia. The study of blood sera of donors was carried out for the presence of IgG antibodies to H.pylori infection in the laboratory of the St. Pasteur.

DETERMINATION OF THE ANTIBODIES OF IgG TO HELICOBACTER PYLORI INFECTION:

The method is based on enzyme-linked immunosorbent assay (ELISA), the result was expressed in international units. The test system "ImmunoComb II H.pylori IgG" was used. The results were assessed according to the scale attached to the test system. According to the level of antibodies, sera were divided into the corresponding groups. 0-19 U/ml-negative result, 20-39 U/ml - low level of antibodies 40-90 U/ml-medium level of antibodies, 91-120 and more U/ml -high level of antibodies.

Statistical processing of the results obtained included the analysis of standard criteria. X²-square was used to assess the significance of differences in the occurrence of certain signs between the control group and patients with multiple myeloma. Determination of the "p" value corresponding to the found value. X²-square, was carried out according to a computer program, taking into account one degree of freedom. All mathematical calculations and general statistical analysis of the obtained studies were carried out using a personal computer using a software package for spreadsheets - "Microsoft-ExcelM Version 7.0 for Windows 95, for Windows-2010, Statistica-5.

RESULTS AND DISCUSSION:

Patients were diagnosed MM based on standard small and large criteria: in the presence of plasma cells in the bone marrow puncture, more 10%, M-gradient in blood /or urine and osteo-destructive lesions in flat bones, the presence of increased immunoglobulin parameters [8; 9], as well as according to a simplified and minimally unchanged diagnostic criteria scheme proposed by the International Working Group for the Study of Myeloma IMWG-International Myeloma Working Group [10; 11].

Considering, that in the normal vital activity of the body and at conducted us studies to identify IgG antibodies to H. pylori in primary patients with MM, in detailed, thorough interrogation, we had a medical history of chronic stomach pathologies study in remission, but clinical manifestations were noted in the form of hungry, nocturnal pains in the epigastria region, at eating rough food and in the form of dyspeptic manifestations.

After established the diagnosis of MM, the patients received targeted therapy depending on the stage of the disease, the immunochemical variant and the severity of the condition. Among patients at detection of IgG antibodies to H. pylori and availability in anamnesis of gastrointestinal tract pathology (atrophic, erosive, erosive gastritis, gastric ulcer and 12 duodenal ulcer, drug gastritis, steroid ulcers) and the possibility of their exacerbation and complications, simultaneously assigned antibiotic therapy in combination with H2 blockers (De-nol, ranitidine, famotidine), proton pump inhibitors (esomeprazole, omeprazole), antacids (maalox, phosphalugel, almogel).

Spend our studies among patients multiple myeloma of the kirgiz nationality and the Russian-speaking population of the residents of the Kyrgyz Republic (Kirgizia), according to the detection of H. pylori infection at the comparative characteristic have significant the difference, the data of which are presented in Figure 1.

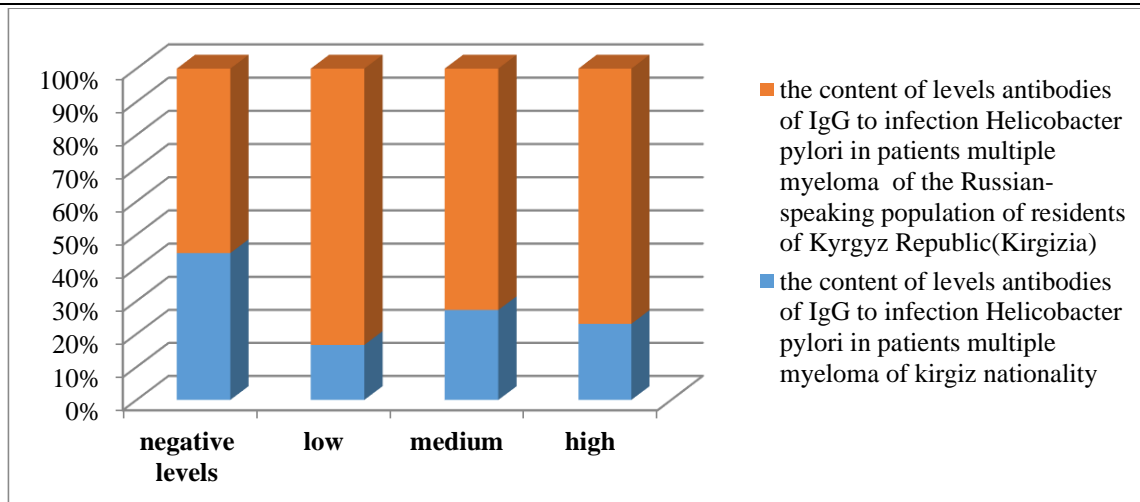


Figure 1. Indicators content of levels antibody IgG to H.pylori infection in patients multiple myeloma of residents Kyrgyz Republic (Kirgizia).

At the comparative characteristic of determining the content of levels antibodies of IgG to infection H.pylori in patients with MM residents of Kyrgyz Republic (Kirgizia), presented on Figure 1, in the our observation showed, that negative levels are detected in patients multiple myeloma of kirgiz nationality in 39% of cases and in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic(Kirgizia) in 61% of cases.

Low levels antibodies of IgG to H. pylori infection among patients with MM of the kirgiz nationality are determined in 11% of cases and in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic(Kirgizia) in 89% of cases.

Medium levels antibodies of IgG to H.pylori infection are detected in patients with MM of the Kirgiz

nationality in 20% cases and of the Russian-speaking population of residents of Kyrgyz Republic(Kirgizia) in 80% of cases.

High levels antibodies of IgG to H.pylori infection are detected in patients with MM of the kirgiz nationality in 16% of cases and of the Russian-speaking population of residents of Kyrgyz Republic(Kirgizia) in 84% of cases.

In the significance of the differences in patients with multiple myeloma of the kirgiz nationality, negative levels antibodies of IgG to H.pylori infection are detected in 39% of cases, and low, medium, high levels are to a lesser degree often detected on comparison with the control group and have statistically significant differences, where $p < 0.005$.

Table 1

Comparative characteristics of the levels antibodies of IgG to H. pylori infection in patients with multiple myeloma of the Russian-speaking population of residents of Kyrgyz Republic (Kirgizia) and potential bone marrow donors of kirgiz nationality.

elicitation of the carrier of infection H.pylori	antibodies of IgG to Helicobacter pylori infection			
	negative	low	medium	high
patients with MM of the Russian-speaking population of residents of Kyrgyz Republic(Kirgizia)	35%	100%	92% *	93%
potential donors hematopoietic stem cells of kirgiz nationality	65%	0% ***	8% ***	7% **

Note: * $p < 0,005$, ** $p < 0,0001$, *** $p < 0,00001$

In a comparative characteristics matching of the results, from Table 1, shown, that in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic (Kirgizia) negative levels antibodies of IgG to H.pylori infection are detected in 35% of cases and in potential bone marrow donors of kirgiz nationality in 65% of cases.

Low levels antibodies of IgG to H.pylori infection in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic (Kirgizia) are detected in 100% of cases and in potential bone marrow donors of kirgiz nationality in 0% of cases.

Medium levels antibodies of Ig G to H.pylori infection are detected in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic (Kirgizia) in 92% of cases and in potential bone marrow donors of kirgiz nationality in 8% of cases.

High levels antibodies of IgG to H.pylori infection are detected in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic (Kirgizia) in 93% and in potential bone marrow donors of kirgiz nationality in 7% of cases

Therefore, on the significance of the differences in elicitation in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic (Kirgizia) levels antibodies of IgG to H. pylori infection low in

100% of cases and levels medium, high in 92-93% of cases on compared with the control group of potential donors hematopoietic stem cells of kirgiz nationality,

and have statistically significant differences, where * $p < 0.005$, ** $p < 0.0001$, *** $p < 0.00001$.

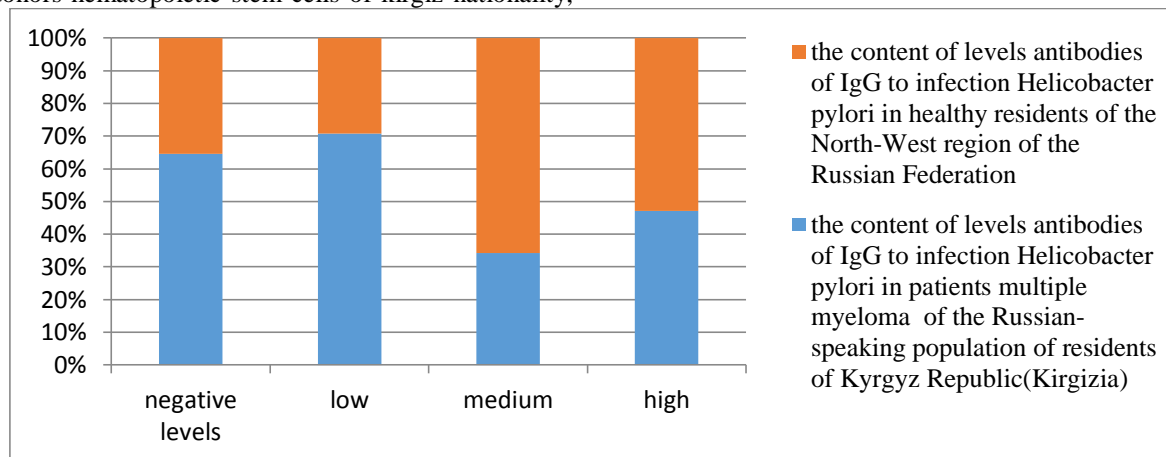


Figure 2. Comparative characteristics of the levels antibodies of IgG to H.pylori infection patients with multiple myeloma of the Russian-speaking population of residents of Kyrgyz Republic(Kirgizia) and healthy residents of the North-West region of the Russian Federation.

As can be seen from the presented Figure 2, shown, that in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic (Kirgizia) negative levels antibodies of IgG to H. pylori infection are detected in 63% of cases and in healthy residents of the North-West region of the Russian Federation in 37% of cases.

Low levels antibodies of IgG to H.pylori infection in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic (Kirgizia) are detected in 70% of cases and in healthy residents by residents of the North-West region of the Russian Federation in 30% of cases.

Medium levels antibodies of IgG to H.pylori infection are detected in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic (Kirgizia) in 34% of cases and in healthy residents by residents of the North-West region of the Russian Federation in 66% of cases.

High levels antibodies of IgG to H.pylori infection are detected in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic (Kirgizia) in 48% of cases and in healthy residents by residents of the North-West region of the Russian Federation in 52% of cases.

According to the significance of the differences, negative and low levels antibodies of IgG to H. pylori infection is more often detected in patients with MM of the Russian-speaking population of residents of Kyrgyz Republic (Kirgizia) on comparison with the control group and has statistically significant differences, where $p < 0.001$.

Table 2

Comparative characteristics of the levels antibodies of IgG to H.pylori infection patients with multiple myeloma and bone marrow donors of kirgiz nationality

elicitation of the carrier of infection H.pylori	antibodies of IgG to Helicobacter pylori infection			
	negative	low	medium	high
patients MM of kirgiz nationality	20%	99%	65%	60%
potential donors hematopoietic stem cells of kirgiz nationality	80%***	1%***	35%**	40%*

Note: * $p < 0,005$, ** $p < 0,0001$, *** $p < 0,00001$

As can be seen from the presented Table 2, in a comparative assessment it is shown, that in patients with MM of the kirgiz nationality negative levels antibodies of IgG to H.pylori infection are detected in 20% of cases and in potential bone marrow donors in 80% of cases.

Low levels antibodies of IgG to H.pylori infection in patients with MM of kirgiz nationality are determined in 99% of cases and in potential hematopoietic stem cell donors 1% of cases, in almost isolated cases.

Medium levels antibodies of IgG to H.pylori infection are detected in patients with MM of the kirgiz nationality in 65% of cases and in potential bone marrow donors in 35% of cases.

High levels antibodies of IgG to H.pylori infection are detected in patients with MM kirgiz nationality in 60% and in potential bone marrow donors in 40% of cases.

By the significance of differences in patients with MM of kirgiz nationality more often the levels of IgG antibodies to H.pylori infection are negative in 20% cases and low levels in 99% of cases, medium in 65% of cases and high in 60% of cases on compared with the control group, where it is necessary to take into account when treating the underlying disease and planning donor blood transfusion and haploidentical(brother, sister) hematopoietic stem cell transplantation and have statistically significant differences, where, * $p < 0.005$, ** $p < 0.001$, *** $p < 0.0001$.

CONCLUSIONS:

Thus, a study for a helicobacter infection in a group of patients with MM and donors hematopoietic stem cells were carried out for timely detection and comprehensive examination during the initial accost. The results of clinical data and laboratory parameters in donors hematopoietic stem cells give it possible to diagnose and allow identify at an early stage the latent carriage of *H. pylori* infection, as well as suspect the disease at the detailed interrogation, which contributes to the timely pushing aside of donors from donation bone marrow. Based on the diagnostic comparative assessment, negative levels antibodies of IgG to *H. pylori* infection are detected in patients with MM of the kirgiz nationality in 20% of cases and in potential donors of hematopoietic stem cells in 80% of cases. At the contraindication to autotransplantation in patients with MM, where possible to carry out haploidentical (brother, sister), closely related, unrelated transplantation of hematopoietic stem cells in the availability of an identical healthy donor that is compatible in all parameters, which have a significant influence on the course, the prognosis of the disease and is of great practical importance.

At the treatment main disease and to achieve a good therapeutic effect from the polychemotherapy, according to the indications of auto-transplantation of bone marrow and for increase the life expectancy of patients, it is necessary to simultaneously investigate and treat in patients MM with pathology of the gastrointestinal tract.

In patients with MM in the detection availability antibodies of IgG to *H. pylori* infection and anamnesis of gastrointestinal tract pathology and the possibility of exacerbation and complications (ulcerative bleeding, secondary anemia, perforation, penetration), it is necessary to simultaneously prescribe antibiotic therapy in combination with H₂-blockers, proton pump inhibitors, antacids. In the period of remission of the underlying disease, according to indications assign schedule modern eradication therapy

FINDINGS:

1. The patients with multiple myeloma and donors necessary be included in the list of studies for helicobacter infection, including to define the levels antibodies of IgG to *H. pylori* infection.

2. In the presence of *H. pylori* infection in patients with MM and donors, necessary to conduct gastroscopy with taking from different maximum of up to 5 (five) ulcerated areas of biopsy material and consultation of a gastroenterologist (oncologist according to indications).

3. In the treatment of the main disease of MM and in the presence of high, medium, low levels antibodies of IgG to *H. pylori* infection, transfer from the intake of tableted steroid drugs to intravenous administration and prescribe eradication therapy during remission, according to indications. After the eradication therapy, it is necessary to no earlier than 4 weeks, conduct controlled

a breath test or to determine titer antibodies to IgG infection of *H. pylori*.

4. To carry out autotransplantation of bone marrow for patients MM with *H. pylori* infection according to indications and in case of erosive, erosive ulcerative gastritis, steroid ulcers, gastric and duodenal ulcers, autotransplantation of hematopoietic stem cells is contraindicated.

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