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Epidemiology of Helicobacter Associated Diseases of Gastrointestinal Tract in Uzbekistan. The Local Treatment Protocols

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Original Research Article

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Abstract: This paper devoted to the results of Helicobacter pylori infection spreading in Uzbekistan, its molecular-genetic characteristics, antibiotic resistance. It is shown that Uzbekistan belongs to the regions with a high degree of infection of the population of the HP. Pathogenic Cag positive bacterial strains were associated with chronic Helicobacter pylori associated gastritis. The resistance of HP to clarithromycin in the region was 13.3%. The effectiveness of the 7-day eradication triple therapy was 65%. Prolongation of the period of eradication therapy to 14 days and the inclusion of a complex of therapies of bismuth preparations allowed increasing the effectiveness of therapy to 95%.

Keywords: HP infection, Cag positive strains, antibiotic resistance.

INTRODUCTION

The multiple epidemiological researches have revealed a wide distribution of the helicobacter (HP) infection – it has covered about 60 % of the population of a planet. D.Y. Graham named a HP-infection as one of the most often meeting human infections [2]. According to the statistical l data at the beginning of XXI century the infection HP is related to the most widespread chronic human infections and meets in 80-90 % of the inhabitants of the developing countries of Asia and Africa, in 40-70 % of the inhabitants of East Europe, of Southern America and in 25-30 % of the population in the developed countries of Europe and Northern America [3].

There are a lot of researches devoted to the link of bacterial factors of virulence and genetic polymorphisms of the host with character of gastritis and risk of the other diseases, in particular of ulcer disease and gastric disease. In a combination with each other they considerably increase risk - for example, in one research it is shown, that in the patients, infected by strains HP, producing vacuolizing cytotoxin (vac A sl), the risk of gastric cancer increases (ratio of chances - 87). In this plan the attention is concentrated on three genetic locuses of bacteria: Cag A, Vac And Ice And. But information about results of these works is rather inconsistent. In Portugal, Italy and Spain VacAsi and Cag A HP are associated with gastroduodenal ulcer disease. In England and France these regularities are not observed. In Asia in a number of works there is shown the domination at the healthy inhabitants of the several countries of Cag A, Vac A strains HP is shown. The dependence of the bacteria properties on the geographic factors brings obvious complexity in this problem [6]. Study on HP in the inhabitants of 20 countries in the world has revealed the certain differences of genotypes. However, the similar investigations in the regions of the Central Asia and, particularly in Uzbekistan, have not been performed to this moment.

The other, not less important problem is the tendency to steady decrease in efficiency of HP eradication up to 70 % at application of standard therapy of the first line, and in some countries - up to 60 % where one of major factors is the problem of antibiotic resistance [1]. The basic antibiotic, to which the resistance has been found in HP appeared to be clarithromycin, which was offered for treatment of infection HP in the beginning of 90-th years of the last century. In the guidelines for HP eradication the use of clarithromycin was not supposed as monotherapy, however attempts to prescribe clarithromycin as unique antibiotic in the eradication schemes resulted in occurrence of resistant strains HP [7]. In the second half of 90-th years the tendencies to fast growth of amount of such strains was noted. If in some countries of the Western Europe the resistance to clarithromycin in the uncured patients accounted only 0-2% and did not influence on the indicators of eradication, however in many centres of Europe achieving 8-15 % and more, in Asia and some countries of Europe the number of resistant strains achieved 60 % [4, 5]. The data about resistance of HP to clarithromycin in Uzbekistan were not obtained that created the certain difficulties in a choice of variants of eradication therapy.

THE PURPOSE OF RESEARCH

Definition of the real covering of the population of Uzbekistan by HP infection and its Cag + and Cag- strains, and also prevalence of resistance to antibiotics in Uzbekistan.

MATERIALS AND METHODS

Materials and methods of research included clinical, biochemical, immunologic, genetic, instrumental methods of research. As a direct method for diagnosis of HP infection there was used CLO - test in biopsies, received at esophagogastroscopy. The respiratory test with labeled C [8] was used as non invasive test for HP determination. A genetic part of researches was performed in the Institute of biological chemistry of the Academy of Sciences of the Republic of Uzbekistan. The genome DNA, stored at temperature -20°C, was material for molecular-genetic investigations of mutations. The mutations were determined with method of PCR in real time with use of primers and probes. For definition of resistance to clarithromycin in the patients with the Hp-associated diseases of gastrointestinal tract there was made Real-Time PCR for revealing of punctuate mutations A2142G/C, A2143G in V functional domain 23 S of pRNA-gene, responsible for formation of resistance of HP to clarihtromycin.

THE RESULTS OBTAINED AND DISCUSSION

The prevalence of HP in Uzbekistan was, on the average, more than 80 % in a population (Fig-1). This allows Uzbekistan to be related to the regions with high degree of covering with HP. There were also revealed 1367 identical genes with European strain HP26695 and 1162 genes identical with genes of African strain J99. These genes make a functional nucleus of genome HP. Two clusters of genes are revealed - zone of plasticity, where the share of strain specific genes makes 79 % for a zone of plasticity HP0423-HP0466 and 37 % for a zone of plasticity HP0982 - HP1028. Among the separate groups of genes responsible for metabolism DNA and proteins of cell membrane were more differed by strain heterogeneity. The geographical distribution of genotypes HP is studied, where in all regions CagA positive variant prevails (Fig-2). VacAs1m1 is met more often in the Khorezm region and Karakalpakstan, VacAs1m2 – in Namangan and Tashkent, in Khorezm there was found great amount (84 %) of mixed IceA1/IceA2 genotype, in the other areas IceA1 allele of this gene prevailed. There were revealed genotypes of a bacteria associated with various diseases of gastrointestinal tract. In expression of gastritis there is prevailed strain - Cag + VacA s1 VacA m2 and IceA 1, in ulcer appearance - strain CagA + VacA s1 VacA m2 IceA 1,2. These researches force to adapt the available standards of diagnosis and treatment of the Hp-associated diseases to conditions of region with a high degree of infection with HP and with high level of mutations of CagA negative strains HP, distinguished by a high degree of virulence in the provocation of ulcer disease, atrophic gastritis and gastric cancer.

The definition of HP resistance to clarithromycin was performed with Real-Time PCR for detection of mutations in genes A2142G/C, A2143G. From 30 samples in 4 there is revealed A2142G/C mutation, that accounted for 13,3 % (Fig-3). Mutation A2143G in the investigated samples is not found out. The received data are below limiting values 15-20 % established by the Maastricht consensus reports.

The reduction of efficacy of traditional 7-day "threefold therapy" with use inhibitors of proton pomp, amoxiciclin and clarithromycin was noted all over the world. According to the data of the various authors the efficiency of this scheme of treatment in various regions of the world has already made from 60-up to 78 %, but does not satisfy the requirements of modern gastroenterology, where the bottom threshold of efficiency of eradication makes not less than 80 %. The researches, carried out in our region, have shown, that the efficiency of standard, "threefold" 7-day eradication of therapy has made by results of direct urease test 64 % and by results of the respiratory test 65 %, that we suggested to be as unsatisfactory (Fig-4). The way for resolving of this problem was lengthening terms of eradication to 14 days and inclusion into a complex of eradication therapy of preparation bismuth tripotassium decitrate. The researches have shown, that at the given scheme of therapy it was possible to achieve increase of eradication efficiency up to 96 % by results of urease, and 95 % by results of the respiratory tests (Fig-4).

Thus it is possible to consider that of Uzbekistan relates to regions with a high degree of the population impaired with HP infection (80 %). The study of pathogenic properties of HP has shown, that it is found out in 84 % of the population of Uzbekistan there is found mixed IceA1/ IceA2 a genotype CagA. If the characteristics of mutation of gene CagA to differentiate by separate nosologies in the expression of ulcer disease there are prevailed pathogenic strains CagA + VacA s1 VacA m2 IceA 1,2. In the patients with Hp-associated chronic gastritis of type B the strain Cag + VacA s1 VacA m2 and IceA l prevailed. The indicator of resistance of the HP strains to clarithromycin in patients with HP-associated diseases of gastrointestinal tract accounted for 13,3%. Taking into account the fact that traditional “7-day” “threefold” therapy shows efficiency below than 80 %, lengthening terms of eradication to 14 days and use of bismuth preparations will be optimum.

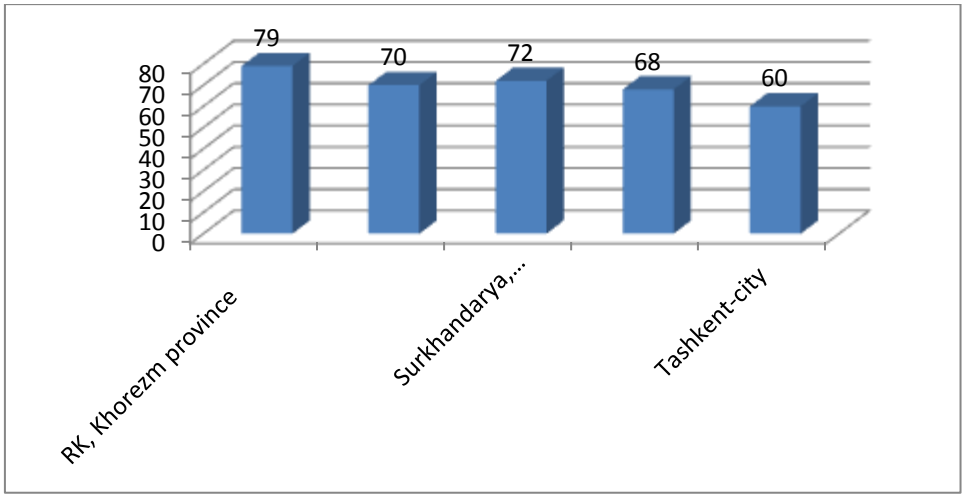

Fig-1: Prevalence of HP-infection in Uzbekistan (%)

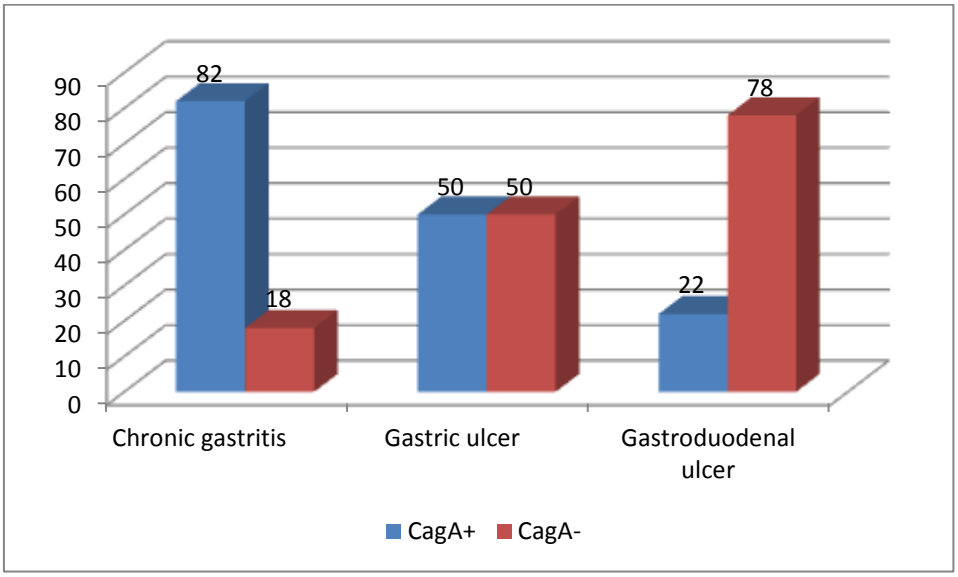

Fig-2: HP virulence factors (CagA-positive strains of allele VacA Slml and VacA s2m2) in Uzbekistan (%)

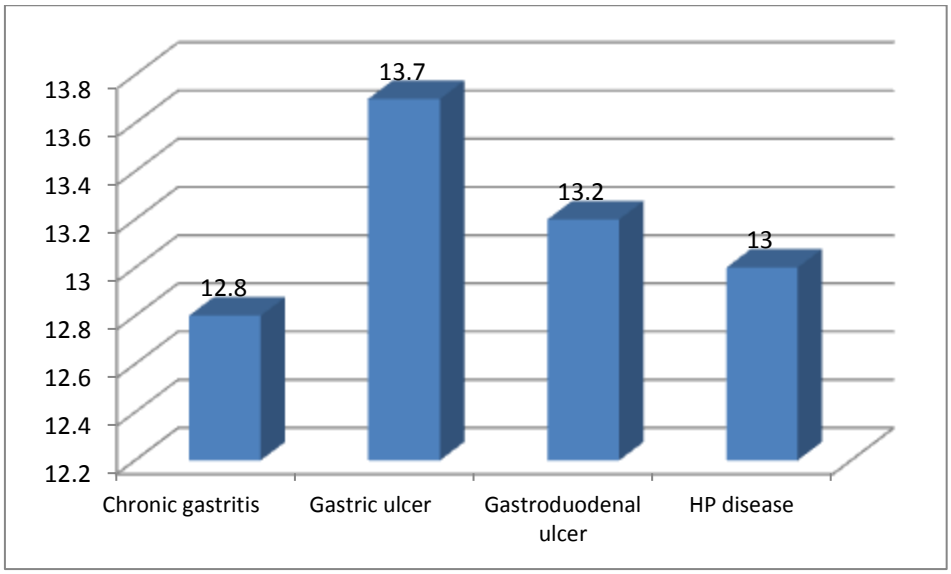

Fig-3: HP resistance to clarithromycin in patients with HP-associated diseases in Uzbekistan of coding gene 23S in mutations A2142G/C, A2143G (%)

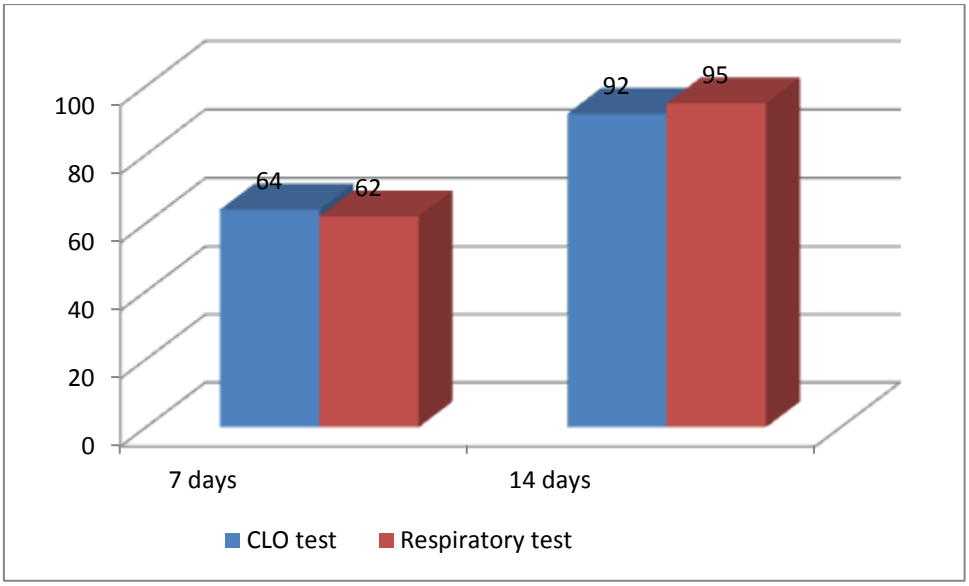

Fig-4: HP infection eradication by results of respiratory test and CLO test (%)

CONCLUSIONS

Uzbekistan is one of the regions of a high degree of the population covering with Helicobacter pylori infection.

Among the patients with the Hp-associated diseases of the gastrointestinal tract the degree of infectivity with Cag positive strains of HP (to 80%) is revealed in the patients with chronic Helicobacter pylori-associated atrophic and non-atrophic gastritis.

The degree of resistance of HP infection to clarithromycin among the patients with Helicobacter pylori-associated diseases of gastrointestinal tract in Uzbekistan makes 13, 3 %, that allows use of therapy of the first line at eradication therapy.

The parameter of eradication efficacy of 7-day "threefold" therapy in the patients with the Hp-associated diseases of gastrointestinal tract in Uzbekistan accounts for, on the average, 65 %, that is much less for effective treatment of HP- infection.

Lengthening terms of eradication therapy to 14 days and inclusion into the complex of therapy of the first line of bismuth preparations according to 5 Maastricht Consensus Report allows to raise efficiency of treatment of the patients with the Hp-associated diseases of gastrointestinal tract to 95%.

REFERENCES

1. Georgopoulos, S. D., Papastergiou, V., & Karatapanis, S. (2012). Helicobacter pylori eradication therapies in the era of increasing antibiotic resistance: a paradigm shift to improved efficacy. *Gastroenterology research and practice*, *2012*.
2. Graham, D. Y. (1998). Antibiotic resistance in Helicobacter pylori: implications for therapy. *Gastroenterology*, *115*(5), 1272-1277.
3. De Francesco, V., Ierardi, E., Hassan, C., & Zullo, A. (2012). Helicobacter pylori therapy: Present and future. *World journal of gastrointestinal pharmacology and therapeutics*, *3*(4), 68.
4. Elviss, N. C., Owen, R. J., Breathnach, A., Palmer, C., & Shetty, N. (2005). Helicobacter pylori antibiotic-resistance patterns and risk factors in adult dyspeptic patients from ethnically diverse populations in central and south London during 2000. *Journal of medical microbiology*, *54*(6), 567-574.
5. De Francesco, V., Zullo, A., Hassan, C., Giorgio, F., Rosania, R., & Ierardi, E. (2011). Mechanisms of Helicobacter pylori antibiotic resistance: An updated appraisal. *World journal of gastrointestinal pathophysiology*, *2*(3), 35.
6. Malfertheiner, P., Megraud, F., O'morain, C. A., Atherton, J., Axon, A. T., Bazzoli, F., ... & El-Omar, E. M. (2012). Management of Helicobacter pylori infection—the Maastricht IV/Florence consensus report. *Gut*, *61*(5), 646-664.
7. O'Connor, A., Gisbert, J. P., McNamara, D., & O'Morain, C. (2010). Treatment of Helicobacter pylori infection 2010. *Helicobacter*, *15*(s1), 46-52.
8. Wu, W., Yang, Y., & Sun, G. (2012). Recent insights into antibiotic resistance in Helicobacter pylori eradication. *Gastroenterology research and practice*, *2012*.