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DEVELOPMENT OF PERIODONTITIS AFTER ANTIHELICOBACTER THERAPY IN PATIENTS WITH ULCER DISEASE

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ABSTRACT

Helicobacter pylori infection is associated with the most common diseases of the stomach and duodenum such as peptic ulcer, gastric cancer, and chronic gastritis. Stomach and duodenum are well-conditioned organs for bacteria. Oral cavity is considered a secondary reservoir of H. pylori. The infection responds well to complex antibacterial treatment, but the risk of recurrence and side effects of this treatment is sufficiently high. This article discusses the H.pylori-related pathology of oral cavity and paradentium, and the side effects and tolerability of eradication therapy. The pathways for optimization of the treatment for H. pylori infection with the use of drugs contributing to the restoration of microflora of the gastrointestinal tract and oral cavity are offered.

Keywords: Periodontitis, Helicobacter pylori, Ulcer disease, Quadrotherapy, Antimicrobial drugs.

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Contribution/ Originality

All authors contributed equally to this work. This study was one of few studies, which have investigated affecting antimicrobial and anti-ulcerative drugs to the development of periodontitis. Authors declare that there is found relations between pathogenesis of periodontitis and treatment of peptic ulcer disease.

1. INTRODUCTION

Currently, therapy for H. pylori is considered the main standard of treatment of peptic ulcer disease (PUD), associated with Helicobacter pylori, which is reflected in the international (I, II, III, IV of the Maastricht Treaty) and Uzbekistani recommendations for treatment of gastroenterological patients. It is known that the problem of Helicobacter pylori infection applies not only to the pathology of the gastrointestinal tract (GIT) but also other related fields, particularly in dentistry, because many authors consider the oral cavity as a possible source of infection of H. pylori and recurrence PUD [1-3]. Active discussion and participation of the mouth in the body reinfection of H. pylori. A number of foreign scientists in their works noted the high likelihood of relapse of ulcerative disease and chronic gastritis associated with H. pylori, because of the incomplete eradication therapy (ET) as a result of the ineffectiveness of some H. pylori by means of insufficient treatment time, preservation of reservoirs of infection, including the oral cavity patients [4].

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In recent years, the contamination of the oral cavity H. pylori began to take into account as a factor influencing the development and course of dental diseases. Discussed the possibility of allocating such terms as H. pylori-associated periodontal disease [5]. In this regard, there is a question about ET as the basic treatment of periodontal disease and gastroduodenal zone (GDZ) in patients with duodenum ulcer disease (DUD) associated with H. pylori [6]. Eradication (destruction) of H. pylori using adequate combinations of antibacterial agents promotes regression of inflammatory-dystrophic changes in the mucous membrane of the stomach and duodenum; restore the protective properties of the mucous membrane of the GDZ; a significant reduction in the frequency of relapses UD (from 60-70 to 1-3 % in the two years of observations), and should thus, and it's complications., to prevent the development of maltoma and stomach cancer [7]. In the presence of H.pylori-associated pathology of gastrointestinal tract goal of treatment is to solve the following problems:

• Troubleshooting in the shortest possible time symptoms of disease;
• The destruction of H. pylori in the gastroduodenal mucosa;
• Mild active inflammation in the mucosa of the stomach and duodenum;
• Ensuring the healing of ulcers and erosions;
• Prevention of exacerbations and complications, including lymphoma and cancer of the stomach.

The number of drugs included in the scheme of eradication, there are:

• Ternary diagram (two antimicrobial antisecretory drugs);
• The four-part scheme, Quadrotherapy (three antimicrobial drug antisecretory).

The use of effective antisecretory funds in patients with ulcer disease (UD) is a great clinical importance, since it leads to reduction of terms of scarring ulcers, getting rid of pain and symptoms of ulcer dyspepsia, significantly reduces the risk of complications. Most importantly and substantially increases the duration of remission, reduces the frequency of recurrence and, therefore, reduce the frequency of recurrence of periodontal diseases [8].

Currently, the most optimal radiation complexes recognized by the scheme, including a proton pump inhibitor (PPI) and 2 or 3 antimicrobial drugs (choice of triple or quadro-scheme treatment depends on the sensitivity of H. pylori in a specific region to clarithromycin) [2, 6]. The decade it took to practice the most effective schemes of treatment. Uncontrolled prescription of antibiotics to achieve eradication in the 1990s has led to an avalanche growth of primary and secondary resistance of H. pylori with consequently reduced efficacy. Illustration of this fact is the resistance to nitroimidazole derivatives are used in most eradication schemes. Multicentre European study to investigate sensitivity to metronidazole in vitro showed that about 27.5 % (from 7 to 49 %) of tested strains were resistant [9]. The threat can be called a rising trend of multidrug-resistant strains was 11.1 %. Obviously, the problem of resistance can only be addressed strictly regulating approach to eradication [9].

It is noteworthy that such high rates of eradication (93.7 %) are logged when you enable the preparation of bismuth in the normal scheme of triple therapy with amoxicillin and clarithromycin. However, the latter combination is preferable, since it allows overcoming the resistance of H. pylori to clarithromycin, the most effective component of ET, and is better tolerated. Amoxicillin impairs the synthesis of glycoproteins in the wall of bacteria and has bactericidal effect against H. pylori, which increases significantly in a neutral environment, drugs inhibit trans peptidase violates peptidoglycan synthesis (a basic protein of the cell wall) during the period of division and growth, causes lysis of the microorganisms. The resistance of H. pylori to amoxicillin develops very rarely. In dental practice, amoxicillin effectively used in the treatment peri-implantation infectious complications, acute and chronic flowing periodontitis, dento-alveolar abscesses and other purulent-inflammatory processes in the maxillofacial region. Amoxicillin is one of the drugs of the first choice in the systemic antibiotic therapy of periodontal disease, can be used prophylactically before an extensive surgery [10]. Numerous studies demonstrate the efficacy of the schemes, including macrolides, with the aim of eradication of H. pylori [11]. Macrolides exhibit

maximum antibacterial effect against H. pylori among all the antibiotics used in the schemes. This effect is dose-dependent and is implemented with the use of clarithromycin at a dose of 1000 mg/day. In the schemes of eradication were used in various antibiotics group macrolides (clarithromycin, azithromycin, roxithromycin) [12].

However, the only clarithromycin due to its pharmacokinetic and pharmacodynamic characteristics present in the recommendations of the Maastricht-II, -III and –IV [13].

In Uzbekistan in eradication, schemes are well-established clarithromycin. According to leading experts, macrolide antibiotics, including clarithromycin, are the most promising group of antibiotics in the treatment of odontogenic infections, including patients with modifications of the immune system that can be widely used in the treatment of periodontal disease. An important issue in anti-Helicobacter therapy is its side effects as well as tolerability and safety of a massive antibiotic therapy in general, which can be allergic, toxic and dysbiotic changes in the body. The frequency of side effects when using various schemes of triple therapy is highly variable and is, according to foreign authors, from 20 to 59 %. Each of the antibiotic itself has many side effects. So, if clarithromycin is possible to moderate dyspepsia – often diarrhea, change in taste, glossitis, etc [14]. The range of such manifestations of amoxicillin is even more pronounced, with a focus on allergic reactions up to anaphylactic shock and angioedema. As mentioned, the third is an antibacterial agent used in the schemes of eradication therapy, is a colloid substrate bismuth. This compound has a pronounced cytoprotective, anti-inflammatory and bactericidal action against H. pylori, however, it is not devoid of side effects. These include a headache, allergic reactions; in addition, when a use of the drug due to the formation in the intestines of a sulfide of bismuth stool is able to acquire a black color that combined with diarrhea may mimic the signs of gastrointestinal bleeding. According to our data, the adverse reaction occurs among 11.7% of patients receiving FL [15].

2. MATERIALS AND METHODS

Clinical monitoring of the condition of the gastrointestinal tract and the oral cavity was based on data from the comparative analysis of the results of applying one - and two-week schemes at the first line of the Maastricht-III. The first group received therapy according to the following scheme: Rabeprazole 20 mg 2 times a day clarithromycin 500 mg 2 times a day amoxicillin 1000 mg 2 times a day course of 7 days. The second group received identical treatment, but within 14 days. The results of the ET was as follows: 83.4% of eradication in patients of the first group and 96.7% of the other that testifies to the greater efficiency of therapy, prolonged to two weeks. Overall, 7 (11.7 %) patients of the first and second groups, respectively, 3 and 4 (of 10.0 and 13.3 %) patients, on the background of the ET noted the symptoms of dyspepsia because of the application of its components. It was a phenomenon of moderate bitterness in the mouth in the morning as in 7-day and 14-day courses (2 cases) and 3 cases of unstable stool (diarrhea) in one patient on the background of a week of treatment and two patients when conducting a two-week eradication therapy. It should be noted that all of these side effects of H. pylori therapy did not result in discontinuation of treatment were successfully stopped taking dioctaedric Smectite 1 packet in 1.5 hours after eating and at night, and did not recover after the course of eradication of H. pylori. By the time the control of eradication (6-week), all these phenomena disappeared [15].

The sharp increase worldwide in the number of H. pylori strains resistant to Nitroimidazoles made it urgent to search for more effective modes of eradication of the microorganism [16]. In this regard, the most effective in regions with low H. pylori resistance to clarithromycin remains the scheme on the basis of a combination of PPI, a macrolide antibiotic (clarithromycin) and amoxicillin (triple therapy). If the sensitivity to antibacterial drugs in a particular individual before treatment was not determined, but the resistance to clarithromycin in the region exceeds 16 %, triple therapy should not be assigned: it is recommended to assign quadrotherapy. Quadrotherapy exists in two versions: classic (PPI+bismuth subcitrate + tetracycline + metronidazole) and a modified first-line

therapy, which in addition to PPI, amoxicillin and clarithromycin included a third component of the antimicrobial formulation of bismuth. Classic quadrotherapy with the preparation of bismuth as a first line therapy leads to eradication in 93.3 % of cases [17].

Therapy Secondary Line [18]

Quadrotherapy

Omeprazole 20 mg 2times per day or,

Lansoprazole 30 mg 2 times per day or,

Pantoprazole 40 mg 2 times per day +

Bismuth subsacylate/subcitrate 120 mg 4 times per day,

+ Metronidazole 500 mg 3 times per day,

+ tetracycline 500 mg 4 times per day.

3. RESULTS

Overall, our experience of the use of clarithromycin and amoxicillin indicates good tolerability of these drugs as under 7-day and 14-day eradication therapy, allowing for proper treatment in almost 100% of the affected patients without any serious consequences. The use of Rabeprazole in the treatment of PUD as the basic drug first-line therapy by the Maastricht III in modes 7 and 14-day treatment has some advantages over the antisecretory drugs of previous generations, due to more strong, fast, long lasting and fairly predictable antisecretory effect. This group of drugs had side effects, their use of resistance and the syndrome is not marked. The second recognized problem in antibiotic therapy is the development of dysbiosis of the oral cavity and the gastrointestinal tract. It is known that irrational antibiotic therapy, adverse environmental conditions, increased stress factors create the conditions for widespread distribution of dysbiosis of the gastrointestinal tract, activation of technical bacterial infections, sensitization of the organism of adults and children. It was proved a significant influence dysbiosis and immunodeficiency, the duration, and severity of acute and chronic diseases of the oral cavity, difficulty and increase the cost of their diagnostics and treatment.

4. DISCUSSION

The traditional complex treatment of a periodontal disease includes the use of general and local antiseptic, antimicrobial, antibacterial preparations of a wide spectrum of action. In most treatment, regimens include antiseptic containing Chlorhexidine, a bacteriostatic effect. It is known that the use of this antiseptic in for 2 weeks leads to disruption of the composition of the microbial flora of the oral cavity, increasing frequency separation and the number of yeast fungi like Candida, which can be interpreted as a subclinical stage of dysbiosis [19, 20]. According to some leading scientists, of periodontal disease on the background of dysbiotic shift in the gastrointestinal tract and oral cavity have the following features [21]:

• earlier than among individuals without background pathology, the generalization of the pathological process;

• more pronounced signs of inflammation in the periodontal tissues, often accompanied by the secretion of pus from periodontal pockets;

• recurrent nature of the course of periodontitis in patients with combined pathology of the digestive tract and mouth;

• resistance to conventional therapy;

• instability remission of the disease.

Thus, the development of dysbiosis in the oral cavity is the most powerful factor contributing to the development and maintenance of periodontal diseases [22]. As a secondary pathology, dysbiosis of the oral cavity

exacerbates the severity and worsens the prognosis of the underlying process, and the successful elimination of dysbiotic disorders improves the results of treatment of primary disease.

Modern approaches to the treatment of chronic diseases of the oral cavity account for complex application etiotropic, pathogenetic and symptomatic therapy. The correction of dysbiotic disturbances in the composition of the comprehensive treatment should include drugs that help restore the microecology and normalization of local immunity [23].

The use of microbial biological products, the active principle of which is the normal microflora with high antagonistic and enzymatic properties, is a promising direction in the treatment of periodontal disease. Depending on the components, they are divided into vaccines, dietary supplements, and eubiotics, probiotics, prebiotics. The most promising group of drugs, mechanism of action which aimed at the restoration of colonization resistance, in general, can be considered immunomodulators of bacterial origin [24]. Lysates of microorganisms, as a representative of the specified class of drugs represents a polyvalent antigenic complex, the range of which corresponds to the traditional representation of the species of causative agents of infectious processes in the oral cavity, increase the phagocytic activity of macrophages, increases the content of lysozyme and interferon, stimulate the production of secretory immunoglobulin A of immune cells, inhibit the synthesis of microbial hydrolases; inhibit the formation of sensitized antibodies [10, 11, 13-15, 25]. Lysates of microorganisms thanks to its compatibility with drugs of different groups and can be included in a comprehensive treatment. To restore the microflora used bifidobacteria nutritious diet food. The most popular and largest currently in the world are the yogurts, which include lactic acid bacteria of different species. Eubiotics is the bacterial preparations, the active principle of which are the live freeze-dried culture of microorganisms – representatives of normal microflora. Leading Russian scientists proved that the use of eubiotics significantly improved clinical periodontal status, contributing to the disappearance of edema and hyperemia of the mucous membrane of the gums, reduce bleeding gums, reduce the concentration of pathogenic and opportunistic microorganisms (Staphylococcus, Proteus, hemolytic Streptococcus), restoration of lactobacilli. Probiotics – enzymes that inhibit the growth of pathogenic microorganisms. Probiotics are activators of growth of normal microflora. In diseases of the mucous membrane of the mouth are also widely used prebiotics lactulose drugs that are not digested in the intestine and stimulate the growth of normal flora. Some scientists in the treatment of dysbiosis rely on phagotherapy, previously determined sensitivity to the phage, which are the natural levers of regulation of the population size of microorganisms, the biological constraints. Bacteriophages have a high specificity to pathogenic microorganisms selectively leiroot only specific bacteria., in the absence of the "host" removed from the body and are indifferent towards it, and also have a higher selectivity than the antibiotics [9-11, 16, 17, 26].

5. CONCLUSION

Thus, a comprehensive individual approach, careful monitoring of patients with pathology of the oral cavity, associated with Helicobacter pylori infection, optimal therapy of H. pylori, in which from a large palette to choose the means of improving its tolerability and a positive effect on the condition of the gastrointestinal tract in general and oral in particular and periodontal can greatly facilitate the portability of treatment and to improve the performance of ET.

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