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HELICOBACTER PYLORI AND PEPTIC ULCER DISEASE, AS WELL AS VIEWS ON ERADICATION THERAPY

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✓ ***Resume***

In a simple and short description, we can say that an ulcer is a defect in the mucous membrane. Over time, it penetrates deep into the muscle and serous layers. Without proper treatment, an ulcer can be complicated by bleeding, perforation, penetration, pyloric stenosis and malignancy. Each of the above represents an outcome that threatens the patient's life.

The prevalence of the disease in all countries is about 4-6% of the adult population. With a full medical screening of patients, this percentage increases to 20-25%.

In this review article, the authors described one of the factors that develops an aggressive factor as Helicobacter pylori, its structure, pathogenicity and the mechanism of ulcer formation in the stomach and duodenum. And also examples of the use of eradication therapy according to the Maastricht Consensus V are given.

Keywords: peptic ulcer of the stomach and duodenum, Helicobacter pylori, eradication therapy.

HELICOBACTER PYLORI VA OSHQOZON YARASI KASALLIGI, SHUNINGDEK, ERADIKATSIYA TERAPIYASIGA QARASHLAR

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Buxoro davlat tibbiyot institute,
Tibbiyot xodimlarining kasbiy malakasini oshirish markazi

Rezyume

Oddiy va qisqa ta'rifda yara kasalligini shilliq qavatdagi nuqson deb aytishimiz mumkin. Vaqt o'tishi bilan u mushak va seroz qatlamlarga chuqur kiradi. To'g'ri davolanmasa, yara qon ketish, teshilish, penetratsiya, pilorik stenoz va malignizatsiya bilan murakkablashishi mumkin. Yuqoridagilarning har biri bemorning hayotiga tahdid soladigan natijani anglatadi.

Barcha mamlakatlarda kasallikning tarqalishi kattalar aholisining taxminan 4-6% ni tashkil qiladi. Bemorlarni to'liq tibbiy ko'rikdan o'tkazish bilan bu ko'rsatkich foiz 20-25% gacha ko'tariladi.

Ushbu sharh maqolasida mualliflar agressiv omilni rivojlantiruvchi omillardan biri Helicobacter pylori, uning tuzilishi, patogenligi va oshqozon va o'n ikki barmoqli ichakda yara hosil bo'lish mexanizmini tasvirlab berildi. Shuningdek, Maastrixt konsensus V bo'yicha eradikatsiya terapiyasidan foydalanish misollari keltirilgan.

Kalit so'zkar: oshqozon va o'n ikki barmoqli ichakning peptik yarasi, Helicobacter pylori, eradikatsiya terapiyasi.

HELICOBACTER PYLORI И ЯЗВЕННАЯ БОЛЕЗНЬ, А ТАКЖЕ ВЗГЛЯДЫ НА ЭРАДИКАЦИОННУЮ ТЕРАПИЮ

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✓ ***Резюме***

Простым и коротким описанием можно сказать, что язва — это дефект слизистой оболочки. С течением времени она проникает в глубь, поражая мышечный и серозный слои. Без корректного лечения язва может осложниться кровотечением, перфорацией, пенетрацией, стеноз привратника и малигнизация. Каждое из перечисленных представляет собой исход, который угрожает жизни пациента.

Распространенность заболевания по всем странам составляет около 4- 6% взрослого населения. При полноценном медицинском скрининге пациентов этот процент увеличивается до 20-25%.

В данный обзорной статье авторы описали один из факторов развивающий агрессивный фактор как Helicobacter pylori, его структуру, патогенность и механизм образования язвы в желудке и двенадцатиперстной кишки. А также приведены примеры применения эрадикационной терапии по Маастрихтскому консенсусу V.

Ключевые слова: язвенная болезнь желудка и двенадцатиперстной кишки, Helicobacter pylori, эрадикационноя терапия.

Relevance

There are quite a lot of works devoted to the pathogenesis of peptic ulcer, as well as in the etiology of its development, but there are many unresolved issues in the etiology. In 1983, pathologist J. Warren and gastroenterologist B. Marshall published data that spiral-shaped bacteria similar to Campylobacter were found on the surface of the stomach of patients suffering from gastritis. And they expressed the opinion that the bacterium is the causative agent of gastritis [4, 23].

Morphologists, on the other hand, determined them in biopsy specimens of their stomach, but no importance was attached to this and they were not considered as an etiological factor. There are a lot of publications about the structure and function of these bacteria, as well as their role in the etiology of gastritis and peptic ulcer disease [14, 16, 19]. In terms of their structure, RNA sequence, and fatty acid composition, these bacteria differed significantly from other Campylobacters and because of this, in 1989 they were called Helicobacter pylori (HP). The meaning of the term reflects two morphological features of the bacterium: "helical" - in vivo they are spiral, "bacter" - rod-shaped in vitro [4].

HP infection routes are oral-oral and fecal-oral. They can also be transmitted from person to person, which indicates intrafamilial carriage (infection). HP is transmitted through water, food, meal and etc. [13].

On microscopic examination after staining a smear with HP according to Gram, you can see an S-shaped or V-shaped form with a size of 0.5-3.0 mcm. At one end of the HP there are from 4 to 6 flagella, which are covered with a mucinous membrane [23,37].

One of the most significant biochemical properties for HP is oxidase, catalase, urease activity and the formation of hydrogen sulfide. The most characteristic feature of a bacterium is the synthesis of a large amount of urease, which ensures its vital activity, as well as a pathogenetic role in damage to the mucous membrane of the stomach and duodenum (DUD). Urease breaks down the urea of food products and, thanks to this, HP surrounds itself with NH_3 and carbon dioxide, guaranteeing itself protection from hydrochloric acid of gastric juice. Before the detection of HP, there was already evidence that the stomach of mammals has the enzyme urease. A few decades after the detection of urease in the stomach, it was found that its activity is associated with the vital activity of bacteria. The bacteria produce so much urease that it accumulates in the tissues of the stomach, which was shown by the study of biopsies of the gastric mucosa [16, 23, 28]. When studying HP in histological and cytological preparations, three degrees of seeding of the mucous membrane can be distinguished [3, 20]:

- weak degree (+) - up to 20 microbial bodies in the field of view;
- medium degree (4-+) - up to 50 microbial bodies in the field of view;
- high degree (4- + +) - more than 50 microbial bodies in the field of view.

HP, producing a large amount of superoxide dismutase and catalase, prevent phagocytosis, which is another wired mechanism. By synthesizing a protease, HP protects itself from being destroyed by hydrochloric acid, and changes pH to neutral. These data show that HP is "perfectly" adapted to life in the stomach. The presence of flagella and a spiral shape allow them to quickly pass through the layer of parietal mucus and penetrate through intercellular contacts. This sequence leads to a decrease in the content of mucoid in epithelial cells [2, 5].

HP is usually detected in the antrum of the stomach. But there is evidence that it is detected in the

fundus, but unlike the pyloric region, where HP is associated with gastritis, colonization of the fundus does not lead to gastritis. It is also found in the duodenum, but in areas where there is gastric metaplasia [14].

HP damaging the epithelium of the stomach and its subsequent proteolysis against the background of chronic gastritis eventually leads to an ulcer. The study of formed ulcers made it clear that HP occurs only at some distance from the ulcer in areas of active gastritis. At the edges of ulcers, HP is not detected, due to the presence of a young regenerating epithelium, which practically does not synthesize mucus [7, 19].

It was determined that HP is not detected on the intestinal epithelium, and ulceration in the intestine is explained that the edges of duodenal ulcers are formed by the gastric epithelium. Quite a lot of HP is detected on such epithelium. Due to the action of relatively high concentrations of hydrochloric acid on the duodenal mucosa, it leads to the formation of gastric epithelium in the duodenum associated with metaplasia, which can be considered as an adaptive process.

Gastric metaplasia often occurs with active duodenitis with hypersecretion of hydrochloric acid, which can be considered as a pre-ulcerative condition [8].

Given the damage to the metaplastic HP epithelium and the impact on it of one of the aggressive factors such as gastric juice, resulting in ulceration of the mucous membrane. At the same time, HP acts as a factor that damages the barrier, and therefore plays a certain role in breaking the balance between aggression and defense. However, the role of HP does not end with the violation of defense mechanisms; in addition, HP enhances the factors of aggression. HP synthesizing urease breaks down urea forming ammonia disrupts the negative feedback system in the regulation of hydrochloric acid secretion. It has been determined that physiologically the secretion of gastrin is inhibited with sufficient “acidification” of gastric juice, its alkalization leads to the activation of gastrin-producing cells and, due to this, to stimulation of the secretion of hydrochloric acid by parietal cells. Continuous synthesis of hydrochloric acid leads to adhesion of parietal cells and is a serious factor in the increased risk of developing duodenal ulcers, significantly lowers the pH of parietal mucus in the antrum [22, 27].

This leads to the neutralization of HC1 and, thus, to a decrease in its inhibitory effect on gastrin secretion. Violation in the negative feedback system is the cause of hypergastrinemia, which, in turn, causes hypersecretion of HC1 and hyperplasia of parietal cells [4, 8, 13].

The mucous membrane of the duodenum under the influence of acidic gastric juice in certain areas undergoes gastric metaplasia. HP, colonizing the mucous membrane of the antrum of such patients, in mucous overlays move to the duodenum, where they can be located in areas of metaplasia and cause their damage. The concept of HP infection of metaplasia sites makes it possible to understand why a pre-ulcerative state does not always end in the formation of a chronic ulcer. HP is the necessary factor that makes it possible for a pre-ulcerative state to turn into a peptic ulcer.

On this basis, D. Gahan proposes to add a new one to the classic formula “no acid - no ulcer”: “no Helicobacter pylori - no ulcer” [12].

Considering that HP is directly related to peptic ulcer disease, the successful treatment of patients with antibacterial drugs, as well as the bismuth drug de-nol, which destroys HP, also testifies. It cannot be ruled out that the persistence of HP on the mucosa is one of the reasons for the recurrence of the disease. And indeed, in patients treated with de-nol, ulcer relapses occur much less frequently [2].

However, it is still impossible to attribute peptic ulcer to chronic infections and thereby solve the problem of its etiology [26]. HP alone, of course, is not enough to form a chronic ulcer. Undoubtedly, the importance of genetic, neurohumoral and, possibly, other factors remains, but it should be recognized that at present there are grounds for talking about the role of the infectious agent - HP. But HP can be pathogenic only in some patients who have certain conditions for this. These include, first of all, the insufficiency of immune and protective mechanisms in the mucous membrane.

Ulcers in the gastric mucosa (GM) and duodenum mucosa (DUDM) are formed as a result of the predominance of aggressive factors (mainly hydrochloric acid and pepsin) over the protective properties of gastroduodenal CO (secretion of mucus and bicarbonates, local synthesis of prostaglandins, integumentary epithelium with sufficient regeneration, preservation of blood supply and etc.) [6, 30].

Strengthening of endogenous factors of aggression (excessive acid formation) and weakening of the resistance of the gastroduodenal mucosa are due to the colonization of the coolant and DUDM by spiral bacteria, which are called HP, and not the action of such factors of aggression as smoking, stress, malnutrition, strong alcoholic beverages, weighed down by heredity, as previously thought.

Helicobacteriosis is one of the most common human infections, which causes the development of gastritis and duodenitis and is the leading pathogenetic mechanism of gastric and duodenal ulcers, low-grade gastric lymphoma and stomach cancer. This must be taken into account when prescribing antibiotics and evaluating their effectiveness [18].

In this regard, the principle of drug therapy for gastric ulcer and duodenum ulcer should be the mandatory use of drugs with both anti-acid and antibacterial activity. [9, 11].

Modern anti-acid preparations reduce the aggressive effect of hydrochloric acid and pepsin on GM and DUDM: rapid relief of symptoms of the disease, scarring of ulcers, creation of an optimal intragastric pH for the local action of most antibacterial agents. But when using proton pump blockers in the form of monotherapy, HP translocation from the antrum to the body of the stomach is possible, which reduces the effect of anti-Helicobacter pylori therapy [1].

Eradication of HP with the help of adequate combinations of antibacterial agents contributes to the regression of inflammatory-dystrophic changes in the gastric mucosa and DUDM, the restoration of the protective properties of the gastroduodenal mucosa, a significant reduction in the frequency of relapses of PU, and, consequently, its complications, and the prevention of the development of lymphoma and stomach cancer [5].

Domestic and foreign scientific and clinical experience has shown that in the treatment of patients it is advisable to use only those drug combinations and treatment regimens that ensure the destruction of bacteria with a course of treatment of 7-14 days in at least 80% of patients and do not lead to the development of side effects requiring withdrawal of therapy [21, 31].

In 1994, a conciliation group of the National Institutes of Health from the United States developed recommendations for eradication therapy in patients with peptic ulcer.. Later, in 1996 in Maachstricht (Netherlands), these recommendations were standardized [23, 30].

The appointment of antisecretory and antibacterial drugs as eradication therapy is explained by the following reasons [1]:

- some antibiotics active against HP are less stable in an acidic environment and their effect is potentiated by antisecretory drugs;
- for ulcer healing, a low level of intragastric acidity is required, which is achieved by taking antisecretory drugs: antagonists of H2-histamine receptors, proton pump inhibitors [17],

Proton pump inhibitors act directly on the H + K + -ATPase of the parietal cells of the stomach, blocking the production of hydrochloric acid, and also have a very weak effect on HP [25 31].

Metronidazole, tinidazole, clarithromycin, amoxicillin, tetracycline, colloidal bismuth subcitrate (CBS) have antihelicobacter activity [25, 30].

Metronidazole and tinidazole - damage the DNA of bacteria, inhibit their replication. They are the basic preparations of three- and four-component eradication schemes. Metronidazole is prescribed at 250 mg x 4 times a day or 500 mg x 2 times a day. Tinidazole 500 mg x 2 times a day after meals for 7-14 days. With monotherapy, HP resistance is observed.

Clarithromycin has a bacteriostatic effect on HP by inhibiting protein synthesis in bacterial ribosomes. It is prescribed at 250 or 500 mg x 2 times a day at the end of a meal for 7-14 days. When using the drug as a monotherapy, HP resistance is sometimes observed to it.

Amoxicillin, disrupting the synthesis of glycoproteins in the bacterial wall, has a bactericidal effect on HP, which increases significantly in a neutral environment. The drug is prescribed 500 mg x 4 times a day or 1000 mg x 2 times a day for 7-14 days at the end of a meal. Resistance rarely seen.

Tetracycline has a bactericidal effect on HP due to the suppression of bacterial cell protein synthesis. The drug is active at low pH values. There is no resistance to the drug. It is prescribed 500 mg x 4 times or 1000 mg x 2 times with meals. Course of treatment 10 - 14 days.

Bismuth compounds, especially colloidal subcitrate (de-nol), are topical preparations. They interfere with HP adhesion to the mucosal epithelium and destroy the integrity of the bacterial wall. Assigned 120 mg x 4 times a day or 340 mg x 2 times a day on an empty stomach 30 minutes before meals, or 2 hours after meals for 7-14 days. Bismuth salts are used to relieve symptoms of dyspepsia, bismuth has a weak antibacterial effect against HP. The antimicrobial activity of bismuth salts is explained by their water solubility. Their other advantage is the ability to heal defects of the gastric mucosa and increase its protective properties.

In HP-associated peptic ulcer, a one-week three-component therapy, including an H + K + -ATPase blocker in combination with two antibiotics, and a four-component one, including an H + K + -ATPase blocker or, less commonly, an H_2 blocker, are recognized as highly effective eradication regimens. - histamine receptors in combination with a bismuth preparation and two antibiotics [22,

27].

The scheme of one-week three-component eradication therapy using an H + K + -ATPase blocker includes omeprazole 20 mg x 2 times a day or lansoprazole 20 mg x 2 times a day in the following combinations - or with metronidazole 500 mg x 2 times a day and clarithromycin 250-500 mg x 2 times a day, either with metronidazole at the same doses and amoxicillin 500 mg x 3 times a day or 1000 mg x 2 times a day, or with clarithromycin 500 mg and amoxicillin 1000 - both drugs are taken 2 times a day.

One-week four-component therapy includes an H + K + -ATPase blocker in a standard dosage in combination with CBS (de-nol), tetracycline 500 mg x 4 times a day and metronidazole 250 mg x 4 times a day. Instead of an H + K + -ATPase blocker, you can use a histamine H2 receptor blocker (ranitidine 150-300 mg x 2 times a day or famotidine 20-40 mg x 2 times a day), and instead of metronidazole, use tinidazole 500 mg x 2 times a day.

The advantages of three-component therapy are the rapid relief of the symptoms of the disease, the low level of side effects. The disadvantages of this scheme are the development of HP resistance to antibacterial drugs during treatment, the translocation of HP from the antrum to the body of the stomach in cases of microorganism insensitivity to the antibiotics used.

The advantages of four-component therapy are their effectiveness even in patients infected with antibiotic-resistant HP strains, preventing the development of HP insensitivity to antibiotics, increasing the protective properties of the GM and DUDM, and the ability to inactivate pepsin. The main disadvantages of therapy are the need to take a large number of tablets and the development of side effects in 30-50% of patients. When using quadruple therapy, HP eradication is achieved in 96% of cases, and when using triple therapy - in 80-90%.

If the ongoing treatment regimen did not lead to the eradication of HP, it should be considered that the bacteria are resistant to the drugs included in this combination. In such a situation, patients with peptic ulcer are prescribed continuous maintenance treatment with antisecretory drugs, and for the eradication of HP, a bismuth-containing scheme of anti-Helicobacter therapy is used, but with a different set of antibiotics. In the absence of the effectiveness of a repeated course of treatment, it is necessary to determine the sensitivity of the HP strain to the entire spectrum of antibacterial drugs used [21, 31].

With the appearance of symptoms characteristic of an exacerbation of peptic ulcer, it is necessary to resume taking antisecretory drugs in a full daily dose for 2-3 days, then in half - 2 weeks.

Supportive continuous long-term therapy with antisecretory drugs in a half daily dose is carried out in patients with a negative effect of eradication therapy, in the presence of reflux esophagitis, with complicated ulcers, if it is necessary to take non-steroidal and other ulcerogenic drugs over the age of 60 years.

HP-associated peptic ulcer recurrences that occurred during the first year after eradication therapy are mainly due to HP reactivation - infections. Re-infection with HP is rarely observed - 3%, occurs at a later date and at the same time genetically different strains of microorganisms are detected.

In peptic ulcer complicated by bleeding, along with endoscopic stop of the latter, intravenous infusion of 40 mg of omeprazole or 100 mg of ranitidine or 40 mg of famotidine in 100 ml of isotonic sodium chloride solution is necessary and immediately proceed, in the absence of contraindications, to ingestion of an appropriate anti-acid drug in combination with anti-Helicobacter therapy. If the ingestion of a combination of drugs is impossible due to severe dyspeptic disorders, then it is necessary to continue the parenteral administration of one of the anti-acid drugs (ranitidine 50 mg, or famotidine 20 mg, or omeprazole 40 mg) with an interval of 8 hours for 3- 5 days, and then carry out the antiulcer therapy indicated above.

Conclusions

Thus, modern medical course therapy for GU and DU can ensure a relapse-free course of these diseases and save patients from possible severe complications.

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