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Pharmacotherapy of Gastropathy (Literature Review)

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Abstract: Disruption of secretory and movement activity of the gastrointestinal tract is observed in many diseases and pathological conditions. A large arsenal of drugs is used to normalize the functions of the gastrointestinal tract. It mainly contains substances that directly affect the secretory and movement functions of the stomach and intestine, as well as the excretory function of the pancreas and liver. At the same time, they include appetite suppressants, as well as anti-vomiting and anti-vomiting drugs.

Keywords: gastropathy, M-cholinoblockers, Proton pump inhibitors pathogenesis, Misoprostol, Rebamipid, De-nol, Vonoprazan, Gastrocytoprotectors

Introduction.

M-cholinoblockers were used as the first antisecretory agents [1]. It has a more or less selective effect on the types of M-cholinergic receptors. In the 60s of the last century, atropine and scopolamine drugs were used in the treatment of peptic ulcers. Decreased secretion under the influence of atropine was observed primarily in the reduction of the volume of secreted gastric juice, not gastric acidity. Since the therapeutic effect of atropine is achieved by a high level of inhibition of cholinergic receptors, characteristic side effects occur - dry mouth, mydriasis, tachycardia, etc.[2,3]. Pirenzepin (gastrozepin) and telenzepin drugs are classified as selective blockers of M1 receptors located in the gastroduodenal area for acetylcholine. In terms of the strength of the therapeutic effect, pirenzepine is weaker than atropine, but it does not have the toxicity associated with the activation of M2 and M3 receptors [4]. However, recent studies suggest that pirenzepine may act through other molecular mechanisms, as it reduces acetylcholine-stimulated secretion in M1-deficient transgenic mice[5]. Pirenzepine and other anticholinergics may have a gastroprotective effect due to the elimination of spasm in the smooth muscles of the stomach. The drug reduces histamine-stimulated hydrochloric acid secretion by 25%, food-stimulated secretion by more than 50%, pepsin and basal secretion by 25-50% [6]. Pirenzepine does not block the production of protective mucus and enzymes, improves the microcirculation of the gastric mucosa and duodenum, suppresses intragastric proteolysis, that is, it also has a cytoprotective effect. It is known that anticholinergic drugs are now practically not used in the treatment of diseases of the gastrointestinal tract due to the emergence of advanced and safe antisecretory agents. Antagonists of N2 receptors (cimetidine, ranitidine, famotidine, nizatidine, lafutidine) selectively block histamine receptors in parietal cells, as a result of which activation of acid secretion by histamine released by enterochromaffin cells of the stomach does not occur. When using drugs of this pharmacological group, the total amount and acidity of gastric juice decreases, as a result of which the concentration of N + decreases to 68% [7]. It has almost no effect on the motor evacuator activity of the stomach. At the same time, it was found that the activity of N2-histamine blockers against gastric ulcer is more specific than against duodenal ulcer. In addition to the antisecretory effect of N2-histamine blockers, direct antioxidant activity is also characteristic [8]. The gastroprotective properties of cimetidine have been demonstrated in experiments with an indomethacin gastric ulcer model at doses of 10-50 mg/kg, but not in an ethanol ulcer model [9]. N2-receptor blockers also suppress the exocrine secretory activity of the pancreas, so these drugs are used in the treatment of acute pancreatitis. Ranitidine, famotidine and, to a lesser extent, cimetidine also have a cytoprotective effect by increasing the endogenous synthesis of prostaglandins. Under the influence of drugs, the formation of gastric mucus and its protective properties increase (due to the increase in the amount of glycoproteins in its content), the speed of blood circulation and regeneration of epithelial cells in the mucous membrane of the stomach increases.

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For the modern drug lafutidine, the presence of gastroprotective activity mediated by capsaicin-sensitive TRPV1 channels was found [10], and in this regard, ulcer healing during treatment with lafutidine may be superior compared to famotidine [11]. Cimetidine, to a lesser extent ranitidine, can reduce the activity of cytochrome R-450 and R-448 oxidizing system enzymes in the liver and slow down the metabolism of natural, many drugs and endogenous substances, and can increase the effect of a number of drugs (diazepam, anaprilin, theophylline) [12]. When cimetidine is used, hyperprolactinemia, impotence, gynecomastia (breast enlargement), galactorrhea may develop. The antiandrogenic effect of the drug (reduction of potency) is not often observed. This side effect develops when taking the drug in large doses (3-10 g/day) for 1 year [13]. The main disadvantage is, first of all, a gradual decrease in the density of histamine receptors, which leads to the development of addiction and the appearance of a return of secretion when the drug is suddenly stopped. comes, which can cause recurrence of gastric ulcer and accelerate it somewhat[14]. In order to avoid this, it is necessary to gradually reduce the dose of drugs. N2-histamine receptor antagonists are relatively safe drugs and rarely cause strong side effects. Of this group of drugs, cimetidine has the most side effects. Famotidine (Kvamatel 20 and 40 mg tabl.; Kvamatel-mini, tabl. 10 mg; Kvamatel powder for injection, 20 mg) is a more active drug not only than cimetidine (40 times), but also than ranitidine (8-10 times). Compared to previous drugs, the selective effect on receptors is higher. It does not cause the "stop" syndrome. Cytochrome practically does not interact with the R-450 system, does not affect the metabolism of other drugs. Famotidine has antiandrogenic effect and does not affect the prolactin level, does not cause gynecomastia. In clinical practice, N2-histamine blockers have been proven to be quite safe drugs, their long-term use is well accepted by patients. Medicines of new generations (ranitidine, famotidine, etc.) are largely devoid of the shortcomings of the first representative of this group - cimetidine: antiandrogen properties, microsomal enzymes and influence on liver blood flow. The main side effects are headache and dizziness, constipation, diarrhea and skin rash [15]. Another side effect common to all antisecretory drugs is stable pharmacogenic hypochlorhydria, which creates conditions for the spread of various pathogenic bacteria in conditions where the antiseptic properties of gastric juice are insufficient. As a result, in rare cases, patients may develop enteritis, bacterial peritonitis, hepatic encephalopathy, often aspiration pneumonia[16].

Currently, Famotidine (Kvamatel), a third generation of N2-blockers, is actively used for the purpose of antisecretory therapy. This generation group reduces not only basal, but also stimulated secretion and differs from the previous ones in having fewer side effects [17]. According to many years of experience, N2-blockers are used as prophylactic antisecretory agents, reducing the frequency of development of gastroduodenal bleeding [18]. Due to the reduced ability to inhibit stimulated secretion due to tachyflexion (habituation) and the short range of prophylactic aniscretory action, as well as the emergence of proton pump inhibitors, N2-histamine blockers have become secondary in prophylactic antisecretory therapy [19]. It should also be noted that N2 histamine blockers have a vasoconstrictor effect on the blood vessels in the mucosa of the stomach and duodenum, causing a deepening of ischemia in the mucosa and muscle layers [20].

The most effective antisecretory drugs are PNI: omeprazole, esomeprazole, pantoprazole, lansoprazole, rabeprazole. Omeprazole is the first representative of a new type of antiulcer drug that inhibits the function of the proton pump (N+, K+-ATPase) in the parietal cells of the stomach. Omeprazole itself is a weak base and has no effect in a neutral pH environment. However, in the acidic environment of the parietal cell channels, it irreversibly interacts with the N+, K+-ATPase of the membrane due to disulfide bonds and turns into the active metabolite sulfenamide. This explains the highly selective effect of omeprazole on parietal cells, where there is an environment necessary for the formation of sulfenamide. The conversion of omeprazole to sulfenamide occurs quickly (after 2-4 minutes). Sulfenamide, which is a cation, has no absorption properties. Thus, omeprazole is considered a pro-drug [21]. The effectiveness of PNI as prophylactic agents preventing the development of ulcers of various origins, in particular, their high activity against ulcers caused by NSAIDs, although not absolute, has been clinically proven [22]. based on the information on the mechanism of toxic action, it can be concluded that the ability of PNI to prevent damage to the gastric mucosa is associated with a decrease in the aggressive properties of gastric juice, which affects the damaged tissues caused by NSAIDs. Consequently, due to a decrease in the acidity of gastric juice, the ability of NSAIDss to form a protonated form can decrease, they are more lipophilic, pass through cell membranes and have a harmful effect[23]. In studies with high adherence to treatment, continuous use of omeprazole can significantly reduce the risk of gastric bleeding observed during long-term treatment with

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Date of Publication:17-02-2023

NSAIDs and antithrombotic drugs [24]. There is no information about. In contrast, a study of the effect of omeprazole on prostanoid production in experimental rats showed that administration of activated omeprazole suppressed the release of prostacyclin secreted by the gastric fundus (from a concentration of 14.3 ± 4.8 μM to 100 μM) and at high doses extinguished the release of PGE2 (100). Interestingly, administration of omeprazole to rats at a dose of 10 mg/kg for 29 days resulted in increased sensitivity of the duodenal mucosa to the toxic effects of ethanol. This the effect is undoubtedly mediated by prostaglandins, because it is aggravated by the introduction of indomethacin, but at the same time, omeprazole does not affect the production of PGE2(14). In general, PNIs have low toxicity and, unlike N2 histamine blockers, do not cause symptoms of withdrawal syndrome. Proton pump inhibitors inhibit not only stimulated secretion but also pepsin [6]. It also has a gastroprotective effect and effectively neutralizes the long-term negative effects of anti-inflammatory steroids, anticoagulants and antiaggregants [9,22]. Over the past decade, antisecretory drugs have increased the effectiveness of prophylactic antisecretory therapy from 3% (to 40-60%) due to their high efficacy and low side effects [1,23]. There are no clear data on the results of their use. Proton pump inhibitors occupy a central place among anti-ulcer drugs. This is because, firstly, they are significantly superior to other drugs in terms of antisecretory activity and clinical effectiveness, and secondly, they are used in eradication therapy for the effect of antibacterial agents against Helicobacter pylori. creates a favorable environment [25]. The results of studies confirm the data on the clinical effectiveness of rabeprazole (earlier cessation of symptoms, antisecretory and cytoprotective activity) than omeprazole, which is more specific than omeprazole [3,26].

In statistical studies, there is an excessive prescription of omeprazole without specific medical indications. For example, for elderly patients, this drug is accepted due to its effectiveness in combination with harmlessness and cheapness [27]. At the same time, when prescribing drugs of this group for long-term use, periodic monitoring of the condition of the gastric mucosa is required, which is associated with the development of compensatory hypergastrinemia. In experiments on Mongolian gerbils, intragastric administration of omeprazole at a dose of 100 mg/kg to healthy animals did not affect the condition of the mucous membrane, but N. pylori-associated atrophic gastritis has been shown to enhance the development of adenocarcinoma[28].N. Pylorigastroesophageal reflux disease, the risk of developing atrophic gastritis and adenocarcinoma increases in patients receiving omeprazole (34). A change in the bacterial environment described above was also noted. Long-term PNI use is associated with an increased risk of osteoporosis. For example, patients treated with esomeprazole showed a significant decrease in femur bone mineral density at 12 months [29]. When experimental rats received omeprazole at doses of 20 or 40 mg/kg for 4 weeks, a slowing of bone resorption was noted, possibly from the digestive tract. associated with calcium absorption disorders [30]. In general, with a decrease in the acidity of gastric juice, many micronutrients from food may be insufficiently absorbed: calcium, magnesium, etc. The lack of nutrients associated with digestive disorders in the stomach can cause plastic failure of all organs and systems, resulting in an increased susceptibility of the body to various diseases. A new class of antisecretory drugs is the K+ competitive PNIs. The first drug of this group, vonoprazan, was introduced into clinical practice in Japan in 2015. Vonoprazan interacts with high affinity with the K+-binding center of the proton pump and therefore irreversibly inhibits both active and reserve N+/K+-ATPase molecules[31]. An important safety issue for vonoprazan is also hypergastrinemia due to hypochlorhydria, which develops more often than with the use of "classic" PNIs. In preclinical studies, oral administration of vonoprazan to mice of both sexes for two years at doses of 6 mg/kg or higher resulted in the development of neuroendocrine enterochromaffin-like cell hyperplasia or malignancies [32]. The combination of lafutidine with N2 histamine blockers prolongs the antisecretory effect and reduces gastrin secretion[33]. This result shows the feasibility of combining antisecretory and gastroprotective agents in the treatment of acid-related pathologies of the gastrointestinal tract. Omeprazole effectively suppresses hydrochloric acid secretion caused by basal or any stimulation. It reduces the total volume of gastric secretion and inhibits pepsinogen secretion. In addition, the gastroprotective activity of omeprazole has also been determined, but its mechanism is not clear. The drug does not change the products of Kasl's intrinsic factor. It does not affect the rate of passage of food mass from the stomach to the duodenum. Omeprazole is highly effective in duodenal ulcer, gastric ulcer, esophagitis with peptic ulcer, Zollinger-Ellison syndrome. It is mainly prescribed for drinking.

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Date of Publication:17-02-2023

The drug is well absorbed by the body. Proton pump inhibitors, like N2-blockers, can cause a "discontinuation" syndrome with long-term use [34]. Hypergastrinemia, which develops as a result of a decrease in hydrochloric acid production, leads to an increase in the weight of the lining cells, and after the drug is discontinued, acid production is slightly increased. possible [35]. However, according to some scientists, proton pump inhibitors do not cause the phenomenon of "return" [5]. When drugs of this group are used for a long time, in some cases, in the submucous shell, especially N. Pyloriinfection, hyperplasia of ECL cells (carcinoids) has been found [30]. In general, side effects are very rare — in 1.5-3% of cases [25]. Proton pump inhibitors cause nausea, headache, dizziness, diarrhea, constipation, abdominal rest, cough, abdominal and shoulder pain, skin rashes, sometimes decrease in potency, gynecomastia [15]. In very rare cases, an increase in transaminase activity develops. As a result of achlorhydria, the previously almost "sterile" mucosa of the stomach and 12 6. intestine can become covered with microorganisms (for example, translocation of N. Pylori). When taken for a long time, as a result of suppression of the bone-brain hematopoietic system.

Proton pump inhibitors include pantoprazole. Pharmacological properties and indications for use are similar to omeprazole. Lansoprazole, rabeprazole are similar drugs.

Antacids are often used to reduce the excess acidity of gastric juice. They have basic properties and enter into a chemical reaction with hydrochloric acid of gastric juice and neutralize it. Antacids include sodium bicarbonate, magnesium oxide, magnesium trisilicate, aluminum hydroxide, and calcium carbonate. Fast-acting antacid preparations include sodium bicarbonate (NaNCO3). However, it increases the production of CO2 in the stomach. This causes the stomach to stretch and expand, thereby increasing the secretion of hydrochloric acid as a secondary stimulus. The drug has a short-term effect. Sodium bicarbonate is very soluble in water, very easily and quickly absorbed. Therefore, it is necessary to remember that it leads to systemic alkalosis. When using magnesium preparations, CO2 is not formed. Calcium carbonate, like aluminum preparations, sometimes causes constipation.

Blockers of gastrin receptors have a wide perspective. Initial substances of this type have already been synthesized (for example, proglumide), but they have not yet been applied to practical medicine. This group of drugs includes drugs that increase the resistance of the mucous membrane of the stomach and duodenum to the effects of aggressive factors. The mechanisms of mucous membrane protection include: increasing the resistance of gastroduodenal cells to negative effects, true cytoprotection, increasing mucus production and improving its quality, increasing the production of bicarbonates in mucous membrane cells, improving microcirculation in the mucous membrane of the stomach and duodenum, in mucous membrane cells activation of regeneration processes, mechanical protection of mucous membrane defects [36].

Gastrocytoprotectors can be conditionally divided into 5 groups according to the dominance of one or another mechanism of action. These drugs form a glycoprotein-bismuth complex in the area of erosion and ulcerative lesions in the acidic environment of gastric juice. This creates a protective barrier that prevents re-diffusion of hydrogen ions, which accelerates erosion or wound healing. De-nol is a colloidal subcitrate of bismuth, which has multifaceted effects on the mucous membrane of the brain: It has a local protective effect on the erosion-wounded area[37].

De-nol forms a complex with protein in the injured mucous membrane, acidic environment (pH <4), due to which a protective barrier appears on the erosion and wound surface, and it prevents the action of hydrochloric acid and pepsin. De-nol binds pepsin and bile acids (pN=1.0-2.0) and has a cytotoxic effect. De-nol enhances the local synthesis of prostaglandin E2. Therefore, mucus secretion increases, viscosity is restored, resistance to re-diffusion of hydrogen ions increases; bicarbonate secretion increases, microcirculation and regeneration processes in the stomach epithelium improve. De-nol has a positive effect on reparative regeneration mechanisms. Epidermal growth factor increases accumulation in the wound area and inhibits pepsin-induced degradation.

De-nol has an antibacterial effect against Helicobacter pylori. Colloidal subcitrate of bismuth is absorbed into gastric juice and kills bacteria there (bactericidal effect). The drug sits on the surface of the bacterium, penetrates its wall and cytoplasm, causing structural changes and inactivation of enzyme systems. All this leads to a decrease in the resistance of bacteria to external environmental factors. The antibacterial effect of De-nol is often best shown in an acidic environment (rN=3.0-3.5). In such conditions, bismuth passes through mucous layers and has an antibacterial effect. However, microorganisms are not completely killed,

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recolonization is observed after the drug is discontinued. Therefore, in Helicobacter pylori eradication schemes[38].

de-nol is recommended to be prescribed in combination with antibacterial drugs. Side effects include blackening of the tongue and stool. Dyspeptic symptoms are nausea, vomiting, diarrhea. During long-term treatment, "bismuth" encephalopathy, arthropathy may develop. Sometimes allergic reactions in the form of skin rashes and itching. Prostaglandins are products of essential fatty acids that are part of the cell membrane. Many prostaglandins (G, A, I, etc.) inhibit gastric secretion, reduce acidity and peptic activity of gastric juice, reduce vascular permeability, normalize microcirculation, increase secretion of mucus and bicarbonates.

In practice, PgE, its synthetic counterpart - misoprostol (cytotek) is used. Misoprostol has a similar effect to endogenous PgE produced in the gastric mucosa. The drug binds to the prostaglandin receptors of the parietal cells of the stomach and suppresses the basal, stimulated and lactating secretions[39]. Misoprostol has a special place in the treatment and prevention of ulcers developed against the background of taking NSAIDs and GKS. The effect starts in 30 minutes and lasts for 3 seconds. It is mainly excreted from the body through the kidneys. It is recommended to reduce the dose in case of kidney diseases. Dosage Misoprostol is prescribed 3 times a day during meals and before going to sleep. Side effects: dyspeptic changes, abdominal pain, changes in arterial pressure, menstrual cycle disorders, skin rashes, edema, and drowsiness can be observed. When used during pregnancy, it causes spontaneous abortion. Regeneration promoters (reparants) Solcoseryl is a protein-free extract from the blood of a black cow, which contains factors that improve the use of oxygen in tissues (200%). Solcoseryl improves reparative processes, protects tissues from hypoxia and necrosis, accelerates regeneration processes in wounds, casts, freezing, bedsores [40]. In stomach and duodenal ulcers, 2 ml m/o 2 times a day until the ulcer heals, then 2-4 ml m/o 1 time a day for another 2 weeks. Methyluracil has anabolic and anti-catabolic activity, enhances protein synthesis in ulcer disease, accelerates cell regeneration processes, helps wound healing. The drug is given 500 mg 4 times a day during or after meals. Duration of treatment is 30-40 days. Anabolic hormones increase the balance of nitrogen, reduce the excretion of urea, potassium, phosphorus, sulfur (sera). Appetite improves in patients, body weight increases, convalescence period after some diseases is eased; healing of wounds, casts, injury areas is accelerated. It is the drug of choice in the treatment of especially debilitated patients. Chirganok (oblepixa) and namatak oils are a mixture of carotenoids and carotenoids, tocopherol and glycerides, oleic, linolenic and palmitic acids. Wound is a reparant with a complex mechanism of action on the healing of injection sites. 1 tea spoon is prescribed 2-3 times a day for ulcer disease and esophageal injury. Due to the low effectiveness, these drugs are prescribed as an adjunct to the standard treatment scheme for gastric and duodenal ulcers. Indications Treatment and prevention of gastric and duodenal ulcer gastritis (erosive) Reflux esophagitis Helicobacter pylori eradication , but each of these drugs has its own place and certain indications for prescribing. For example, misoprostol is prescribed to patients with a high risk of ulcer formation for the treatment and prevention of UTI-gastropathies. Sucralfate is the drug of choice in patients with hyperphosphatemia (uremia)[41].

One of the most popular drugs is carbenoxolone Biogastron, a cyclic triterpene obtained from licorice root. Its gastroprotective effect consists in stimulating the production of mucus by the glandular epithelium of the stomach. Activation of glycoprotein secretion is associated with prostaglandins, as carbenoxolone has been shown to inhibit 15-hydroxyprostaglandin dehydrogenase, the key enzyme in prostaglandin metabolism (132). Thus, the effect of carbenoxolone is carried out through prostaglandins. A.E. Chávez-Piña and co-authors also found that the gastroprotective effect of carbenoxolone in a model of ethanol-induced gastropathy in rats was mediated by increasing NO levels. Carbenoxolone to a small extent, but statistically significantly reduces the acidity of gastric juice, which is primarily associated with an increase in bicarbonate production [35,42,43]. According to clinical studies, the gastroprotective and regenerative activity of carbenoxolone is low. Carbonexolone is inferior to cimetidine in wound healing [49]. The main drawback of the drug is its mineralocorticoid activity, which is related to its steroid structure and ability to interact with aldosterone receptors. In this regard, thiazide diuretics are prescribed together with carbenoxolone, reducing side effects, but not reducing gastrointestinal protective activity [47]. Currently, carbenoxolone is not used in the treatment of gastric and duodenal ulcers due to its ineffectiveness and serious side effects. Available since the 1970s, sucralfate (venter) is a basic aluminum salt of sucrose octasulfate that forms a viscous buffer polymer in the acidic environment of the stomach. Due to its ability to adsorb, sucralfate neutralizes the proteolytic effect of

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pepsins, as well as the harmful effect of bile acids on the mucous membrane [45]. In terms of prophylactic effect, sucralfate corresponds approximately to N2-blockers, but at the same time it significantly reduces the risk of developing aspiration pneumonia [46]. In addition to the gastroprotective effect , sucralfate has clear regenerative properties, which are manifested not only in mucosal damage, but also in skin wounds and burns[47]. This effect is due to the presence of sulfated sucrose in the composition of the drug, which is similar in structure to heparan sulfate of the extracellular matrix. Application of this agent has been shown to be associated with increased bFGF concentrations in the affected area, which has an affinity for sulfated polysaccharides, as described above. Thus, sucralfate significantly accelerates repair by stimulating the formation of granulation tissue at the bottom of gastric ulcers [48]. Thus, administration of sucralfate to rats at a dose of 100 mg/kg promotes rapid healing of experimental wounds induced by HCL and ethanol, as well as by PPIs or N2histamine receptor antagonists. increases the rate of regeneration when used together with [49]. Since the discovery of the gastroprotective effect of prostaglandins, their synthetic analogues have been put into practice, which have greater chemical stability and oral bioavailability than the original molecules. The most commonly used drugs are misoprostol (prostaglandin E1) and enprostil (PGE2), but the latter was excluded from clinical practice due to the high frequency of side effects and ineffectiveness [50]. Misoprostol (Cytotec) at a dose of 100 μg/kg has a clear gastroprotective activity against experimental ulcers induced in rats by indomethacin [51] and ethanol (39). At the same time, the area of damage caused by ulcerogens is significantly reduced compared to the administration of omeprazole in doses up to 50 mg/kg. According to the researchers, the therapeutic effect of synthetic prostaglandins is inferior to antisecretory agents, but misoprostol has been shown to neutralize the regenerative process caused by NSAIDss in the acetate wound model in rats and promote the development of granulation tissue [52]. The effectiveness of misoprostol has also been proven in clinical studies. Thus, misoprostol is superior to sucralfate in its gastroprotective activity against NSAIDs-induced ulcers in arthritic patients [53]. However, its prescription and patient compliance are limited by frequent side effects such as diarrhea and abdominal pain. Perhaps, such a negative effect of the drug is due to the interaction with PE4 PGE2 receptors, through their activation, the secretion of chloride ions increases and the absorption of NaCI in the intestine decreases [54]. In addition, it should be remembered that the activity of prostaglandins also extends to the uterine myometrium, and therefore the drug is contraindicated in pregnancy or may be prescribed for medical abortion [55].

This fact is another evidence of the rationality of supplementing antisecretory therapy with gastroprotective agents, whose effects are somehow related to prostaglandins. Rebamipid (Mucogen) According to the description, a new drug whose effect is to activate the synthesis of prostaglandins in the gastric mucosa is rebamipid (mucogen), which was developed in Japan in the 80s. Rebamipide is an α-amino acid derivative of 2(1N)-quinolone. Its therapeutic dose for humans is 300 mg per day. The exact mechanism of activation of prostaglandin production has not yet been studied, but it has been determined that the drug activates SOG-2, mucin synthesis. Reduces inflammatory processes in the gastric mucosa and prevents the activation of neutrophils. In addition, the rebamipid molecule has antioxidant activity against hydroxyl radicals. Currently, rebamipide is successfully used in a number of Asian countries (Japan, China, the Philippines, Vietnam, etc.), it appeared on the Russian pharmaceutical market in 2016. The drug is used in the treatment of functional dyspepsia, chronic gastritis, reflux esophagitis, ulcers caused by NSAIDs, ulcerative colitis, restoration of the gastric mucosa after surgical interventions, and N. It is used to destroy pylori. It was found that rebamipide neutralizes the side effects of omeprazole, suppresses the excessive production of gastrin, and also increases the effectiveness of the treatment of acid-related diseases in combination with PNI. In the treatment of chronic atrophic gastritis with rebamipide, patients showed normalization of the architecture of the gastric mucosa with a reduction in the foci of metaplastic changes (Han X. et al., 2015). With long-term use of rebamipide, side effects characteristic of misoprostol occur less often (less than 1% of all patients) and are less pronounced, which does not prevent treatment discontinuation [57]. However, the drug is contraindicated during pregnancy, but the literature on its effect on the birth of the fetus no data found. Despite the existing shortcomings of existing gastroprotectors, their combination with PPIs or H2-histamine blockers has been repeatedly proven to significantly increase the effectiveness of ulcer prevention and anti-ulcer therapy. For example, using sucralfate, misoprostol, enprostil, lafutidine and rebamipide, gastroprotective agents have demonstrated the ability to neutralize the dangerous side effects of long-term use of antisecretory agents, such as compensatory hypergastrinemia and shifts in the body's bacterial environment

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Date of Publication:17-02-2023

[58]. During the recovery period after eradication therapy and surgical operations, gastroprotective drugs should be prescribed to maintain the protective functions of the gastric mucosa, as well as to prevent complications and recurrence of chronic forms of gastrointestinal tract diseases[59]. Existing synthetic drugs of this pharmacological group undoubtedly have a number of disadvantages related to poor tolerance. One of the ways to solve this problem is to look for protective agents among the components of plant raw materials, because plant products, as a rule, are characterized by versatile biological activity and mostly limited toxicity[60]. Various preparations of bismuth (bismuth subcitrate, bismuth subsalicylate, bismuth subgallate, etc.) have been used and are still used in clinical practice, but currently, bismuth tripotassium dicitrate (De-nol) is the most popular. Traditionally, bismuth tripotassium dicitrate is classified as a cytoprotective agent that increases the resistance of the gastrointestinal mucosa to various aggressive factors. The duration of use of bismuth drugs (as part of eradication schemes and as monotherapy) varies from 7 to 56 days, and the daily dose varies from 400 to 2100 mg. The overall relative risk of adverse events was 1.01 compared to controls (abdominal pain 1.06, stool darkening 5.06, diarrhea 1.01, nausea and vomiting 1.16, general weakness 1.18 , headache 1.31, metallic taste in the mouth 1.02).). The relative risk of early treatment discontinuation due to side effects was 0.86. [61].

Conclusion

It is important that the role of acid peptide disorders, infectious (Helicobacter Pylori) and motor factors underlying the development and recurrence of gastric and duodenal diseases can be influenced by drugs. Usually, these drugs are used in gastric and duodenal mucosal lesions caused by imbalance between hydrochloric acid and pepsin and mutual erosive effects of gastroduodenal mucosal defense mechanisms. Therefore, the main tactic of treatment for such a pathology is to reduce the secretory activity of the gastric glands and increase the cytoprotective mechanisms.

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