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MORPHOFUNCTIONAL CHARACTERISTICS OF GASTRIC MUCOSA IN DOGS DEPENDING ON THE EXPERIMENTAL TREATMENT OF PEPTIC ULCER

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GENERAL DESCRIPTION OF WORK

The relevance of research. Peptic ulcer is found in almost all animal species. Stomach ulcers are registered in the pigs, regardless of their breed and sex (Shalimov V.G., Zharov A.V., 1995; Korobov A.V., 1998; 2002). This pathology is diagnosed in pigs - in 40-50% of the total number of culled animals. In piglets - weaners piglets and yelts incidence of fundus and cardial ulcers of the stomach is 45.5% (Lakovnikov E.A., 1985; 1988). In dogs ulcer has become much more apparent after endoscopy has become a widely used method of diagnosis (Nimand H.G., Suter P.F., 1998; Sadovnikov N.Y., Makarov V.V., 2000; Sadovnikov H.YU., Sobeschanskaya M.O., Lebedev A.V., 2001). History of the study of this disease is quite long. Thus, in 1901 V. Izmentyev described a "round" stomach ulcer in dogs, while N.N. Mari in his book "Fundamentals of pathological anatomy in domestic animals" (1906) highlighted the list of causes and postmortem picture of peptic ulcers. In spite of such a rich history of the study of peptic ulcers and even with the large capacity of modern therapy, the disease often recurs not alone, but also accompanied by the development of dangerous, and sometimes fatal, complications. The frequency of recurrence of the disease reaches 31-38% (Grebenev A.L., Golachevskaya B.C., Kurtyanu B.N., 1985; Bredikhina N.A., Bendikov E.A., Silvestrova C.Yu., 1990; Galanin S.N., Sergeev V.N., 1992; N. Goncharov, Doktorov K.N., 1993; Abramov S.S., Kovalenok J.K.; 1997; Berg C.L., Gollan J.L., 1994).

In the recent years, the practice of Russian veterinary and medicine tends towards greater use of non-traditional methods of treatment, of which laser therapy in combination with the influence with the static magnetic field plays the main role. Experiments and clinical studies have established that laser light reduces the inflammatory response by shortening exudative and proliferative phases of inflammation, stimulates regenerative capacity of tissues, in particular walls of the gastrointestinal tract (Balalykin A.S., Terekhova T., Lapshina V., 1989; Stormy N.A., Fedin V.P., Bashir-zade, T.A., et al., 1990; Danilov N.M., Marchenko N., 1991; Arkin A., 1992; Boyko V.N., 1993, Nikitin R.S., N. Tumanov, 1995; Zimmerman Y.S., Popova N.I., 2000; Novitsky V.A., Kuznetsov V.V., 1996 ; Chayda A.A., Efimova E.G., 2002; Efimova E.G., Lutai A. 2001; Devis G.L., 1995).

In the recent years, in clinical practice, drugs with sorption and detoxification properties similar to enterosorbents are of increasing popularity (Velikanov V.V., 2002). These drugs do not undergo hydrolysis in the gastrointestinal tract, have a shielding effect, and prevent the cell surface from external mechanical and chemical aggressions (Mamaev IA et al., 2000).

Inclusion of immune modulator in the complex therapy of peptic ulcer disease has a positive effect on the clinical course of the disease, promotes more rapid relief of its subjective symptoms, earlier ulcer scarring, and long-term stable remission (Vashchenko V.M., Uspensky V.M., Semenov V.V. et al., 1983, Zimmerman Ya.S. et al., 1998).

However, these studies are clinical, without a thorough research of morphology and function of the digestive organs.

We have formed a hypothesis that the combination of immune modulator, enterosorbent and laser light (LL) in combination with the static magnetic field (PMP) can have significant effects on morphology and status of healthy animals and animals with gastric ulcer.

The present work is a part of a comprehensive research program of the department of state budget of pathomorphology, therapy, obstetrics and surgery of the Institute of Veterinary Medicine and Animal Husbandry of the Far Eastern State Agrarian University "Veterinary well-being" (state registration ID (0.186.0060.935).

Purpose of the study. To study morphological and secretory response of the gastric mucosa to the separate and combined effects of Enterosgel, Ribotan and laser in the static magnetic field in experimental ulcer disease.

To achieve this goal, the following tasks were identified:

1. To investigate the separate and combined influence of Enterosgel, Ribotan and laser in the static magnetic field on the secretory function of gastric glands of healthy animals.

2. To study the changes in the secretory response of the gastric glands in experimental gastric ulcers in dogs.

3. To investigate separate and combined influence of Enterosgel, Ribotan and laser in the static magnetic field on the secretory function of gastric glands in experimental ulcer disease.

4. To study the morphology of microcirculation and lymph flow in the gastric mucosa of dogs in the combined treatment with Enterosgel, Ribotan and laser in the static magnetic field in the experimental gastric ulcer.

5. The morphological structure of the tissue of white blood cells in the gastric mucosa in the combined treatment of Enterosgel, Ribotan and laser in the static magnetic field in the experimental ulcer disease in dogs.

6. To examine the separate and combined influence of Enterosgel, Ribotan and laser in the static magnetic field on the morphology of ulcer, periulcer infiltrate and morphofunctional condition of the stomach walls.

MATERIALS AND METHODS

1. Characteristics of conditions for carrying out experiments

Investigations were carried out in the laboratories of the Institute of Veterinary Medicine and Animal husbandry of the Far Eastern State Agrarian University. Secretory function of the stomach - in the laboratory of the Department of Physiology and Zoology. Morphological studies in experimental pathology - in the laboratory of the Department of pathological morphophysiology, therapy, obstetrics and surgery.

The objects of the study were mongrel dogs weighing 12-15 kg. The animals were housed in a comfortable vivarium of IVMZ Institute equipped with special sections for each animal species.

Depending on the goals and objectives of the study, the dogs were distributed into 15 groups of three animals each. For histopathological studies the animals were divided into six groups considering the duration of experimental stomach ulcer disease (days 8,16,18,20,22) without treatment and with the use of various methods of treatment of this disease: the first and the second – control groups; third, fourth, fifth and sixth – experimental groups.

Secretory function of gastric glands and biopsy were examined on the dogs with fistulae. In animals, a ventricle isolated by the method of I.P. Pavlova was created surgically (I.P. Pavlov, 1946), with preserved nerve connections with the alimentary center. This allowed to obtain clean gastric juice during the experiments, with no contact with food.

The dogs were fed twice a day with porridge, cooked with meat and bone broth with ground cereals and soy flour at 7 a.m. and 4 p.m. Access to water was not restricted. The dogs were walked twice a day before feeding, at the same time wet cleaning was carried out.

Postoperatively, the dogs were kept in the laboratory, following a special diet. Twenty-four hours after the surgery the animals were fed with boiled water, being gradually transferred to milk in the following days, after four days bread was added to the mix. On the sixth day gruel was added to the meat broth, subsequently used as the experimental diet. By days 10-12 the dogs were transferred to a normal twice-a-day feeding. During this period, they were taught to tolerate the in-machine fixation and to the experiment mode, at the same time test experiments were performed. Curves of secretory and enzyme-secreting response of the gastric glands were formed, on the basis of which the readiness of dogs in the experiments was estimated. On the 15^{th} day antral stomach ulcer was simulated by diathermal coagulation of gastric mucosa through fibrogastroscopy (OLIMPUS CLE-4U), followed by administration of vincristine at a rate of 0.01mg / kg for persistent chronic process (S.A. Shalimov, 1989).

2. Morphophysiological research methods

2.1. Physiological research methods

Five series of experiments were carried out on healthy fistuled dogs and five dogs with experimental ulcer. The study design was identical in all the series. After 18 hours of fasting the animals were exposed to one or another factor being studied, fixed in the machines, and for the first hour reference level (background) of secretion was determined. Then the dogs were fed and examined every hour for the next three hours.

In the first experimental series, according to the study schedule, the dogs were forcibly administered Enterosgel at a dose 0.2 g per kg of animal weight. In the second experiment, the dogs were injected ribotan i.m. at a dose 2.0 ml per 20 kg of animal weight. In the third experiment, the stomach area of the dogs were irradiated with laser from the ventral surface of the body on the xiphoid projection in a caudal direction in four zones for 2 min each, at a frequency of 50 Hz and power of 40-45 mW. In the fourth experimental group, the animals received Enterosgel orally, ribotan was injected i.m., at the same time the stomach was irradiated at the same dose and concentration. In the control groups the dogs were fed with distilled water (0.2 ml / kg) at the same dose as Enterosgel. In the fifth experiment hroup peptic ulcer disease was simulated. This group served as a control for the following groups of animals. In the sixth, seventh, eighth and ninth groups the animals were treated with Enterosgel, ribotan and laser radiation, both separately and combined, as in the previous groups.

Tension of secretory activity of the gastric glands was studied by volume of gastric juice secreted and concentration of the main components, such as free hydrochloric acid, the total amount of acids and pepsin. The total secretion of these components was determined by multiplying their concentration by the volume of the collected juice for each hour of the experiment.

2.2. Biochemical research methods

Free hydrochloric acid and a total acidity of gastric juice was determined by titration of 0.1 normal sodium hydroxide solution in the presence of phenolphthalein indicator and dimetilamidoazobenzola. Acid concentration expressed in meq / liter.

Activity of peptic juice was determined by method of N.P. Pyatnitsky (Leia Yu. Ya., 1996). Its concentration was expressed in standard units by Pyatnitsky.

2.3. Methods for histological examination

Histological studies included autopsy and biopsy of materials obtained from the edges and the bottom of the ulcer, periulcerous area, as well as from the fundus, cardia and antrum. Selected material was fixed in 10% neutral formalin aqueous solution. Fixation of tissue specimens was carried out by the usual method (Volkov O.V., Eletsky Yu., 1982), by pouring the material in paraffin. The obtained histological sections were stained with hematoxylin and eosin.

2.4. Morphometric study methods

When performing morphometric study of the stomach, ocular micrometer-MoU 1-15m (GOST 151-50-69) wall used and ocular grid for cytohistostereometric studies with 100 and 25 points equally spaced positions of zero thickness (Avtandilov G.G., 1972; 1973; 1980; 1981 ; 1984; 1990). During the morphometric studies volumetric density (V_i) of the arteries, veins, lymphatic vessels, interstitial spaces, cells and intercellular substance was measured. The number density (N_A) of lymphocytes, neutrophils, eosinophils, mast cells, erythrocytes, monocytes, macrophages, degenerating cells and plasma was measured as well. Type of cells was determined in accordance with the recommendations of Y. Borodin, V.N. Grigoryeva (1986).

2.5. Endoscopy of the upper gastrointestinal tract

Fiberoptic esophagogastroduodenoscopy in experimental animals was carried out by the usual method (Sadovnikov N.Y., Sobeschanskaya M.O., Lebedev A.V., 2001) before modeling chronic stomach ulcers, during modeling and on the eighth day of the experiment. This kind of research was performed for the first time to eliminate the inherent (stenosis, tracheoesophageal fistula, diverticulitis etc.) and acquired (foreign bodies, inflammatory diseases, benign and malignant tumors, trauma, hemorrhage, erosion, ulceration, etc.) diseases of the esophagus and stomach. To this end, during the study took into account the motility of the esophagus and gastric mucosa color, presence of plaque, exudate, bleeding, erosions and ulcers. During the simulation, size and depth of gastric mucosa defect were controlled endoscopically. On the eighth day of the experiment fibroesophagogastroduodenoscopy was performed to control chronic ulcer. At the same time location, shape, size and stage of development of the ulcer, presence of periulcerous infiltrate (perifocal inflammation) and complications were taken into account, as well as state of the gastric mucosa and duodenal ulcer, cardiac and pyloric sphincters. To assess the dynamics of the pathological focus, a special dipstick was applied. Endoscopy of the gastrointestinal tract was performed in the morning fasting, i.e. not earlier than 12 hours after the last feeding, as follows: at the beginning premedication by subcutaneous injection of 0.1% solution of atropine sulphate (0.02 mg / kg) was performed 20 minutes before intramuscular injection of 2% solution rometar (4.5 mg / kg). After the onset of general anesthesia fibroesophagogastroduodenoscopy was performed in experimental dogs with fibrogastroscope OLYMPUS GIF - P30. At the end of the study 10% sulphocamphocaine solution was injected subcutaneously (4 mg / kg).

2.6. Statistical processing of the results

All figures were verified for normality sampling distribution by Kolmogorov-Smirnov test and omega squared ω2. In a normal (Gaussian) distribution of data parametric methods were used for calculation of the sampling mean (M), mean error (m), sample variance and standard deviation. Statistically significant differences of compared values were determined on the basis of Student's t test for independent samples. Differences between mean values were considered statistically significant at $p < 0.05$. Statistical computer processing was performed using the program «Microsoft Office Excel» and «STATICA V.6.0».

STUDY RESULSTS AND THEIR DISCUSSION

The first stage of the experiment was to observe secretion and function of gastric glands in dogs with miniature stomachs when feeding with Enterosgel. The results confirmed inhibitory effect of Enterosgel on secretion of gastric glands, particularly secretory function of the main and parietal cells. In marked decrease of concentration of the components the total juice secretion was also significantly decreased in relation to the benchmarks by significantly reducing the amount of gastric juice. Also, we noted that reaction of the gastric glands on Enterosgel was the most pronounced immediately after administration, that is, from the first hour of observation.

The second phase of our study was to investigate the effect of immunomodulator ribotan on secretory function of gastric glands. Only a few papers were published on immunity in peptic ulcer disease (Vaschenkov VM, 1984; Preobrozhensky VA, et al., 1985; Tarasova GN, 1989; Uspensky VM et al., 1988; Zimmerman YS, Golovanov YS, 1982). The results of use of immunomodulators is ambiguous. In the scientific literature there are no data on the effect of immunomodulators on the stomach secretory function.

In the study of this issue, we found that ribotan does not change secretory function of the main and parietal cells. With an overall downward trend in the concentration of the components, total juice secretion is not different from the benchmarks. Also, we noted that the reaction of the gastric glands was the most pronounced in hungry dogs.

The third step was to study laser impact on the secretory function of gastric glands. Veterinary and medical practice has to date accumulated abundant information on practical laser application for therapeutic purposes. (Belov, AM, 1990; Gorbatenkova EA, 1988; Efimova EG, Lutai AV, Chayda AA, 2001; Zolotarev TA, Oleshko AY, Oleshko TI, 2001; Hanby AN, Playford RJ, 1995). Repeated laser irradiation increased stomach pH in the cavity, and a decrease in the frequency of its rate (Ivashkin VT, 1987; Hachiev LG, 1980). Several authors have noted that laser of different power can both stimulate and inhibit activity of the endocrine cells of the stomach and other glandular cells (Baibekov IM, 1995; Gnidash SG, 1988; Muraviev MF, Savelyev I.N., 1981; Chayda AA, Efimova EG, Kaplan MA, 2002).

From the analysis of our work it is clear that LI in SMF excites gastric glands by stimulating secretory function of the main and parietal cells. With an overall downward trend in the concentration of the components, the total juice secretion was significantly increased in relation to the benchmarks by a considerable amount of juice. Also, we noted that response of the gastric glands to the impact is the most pronounced after feeding the dogs, that is, during the development of the food acrtivation.

As a result of the impact of separate series of experiments with ribotan, Enterosgel and LI we can judge on their different actions on the stomach cancer. Therefore, our next task was to study the simultaneous (combined) effects of ribotan, Enterosgel and laser on the secretory function of gastric glands, as we have suggested that this combination can cause a qualitatively different reaction of glands. The scientific literature provided no information on the subject.

Analysis of the total secretion of gastric juice components in the combined impact of Enterosgel, ribotan and laser over 4 hours of the experiment has shown that the most sensitive are the parietal cells, as concentration of free hydrochloric acid decreased by 61%. Less sensitive are the main gland cells, as pepsin activity was reduced by 46%. Intensity of the total number of acid secretion occupies an intermediate position, and was reduced by 55% (Figure 1).

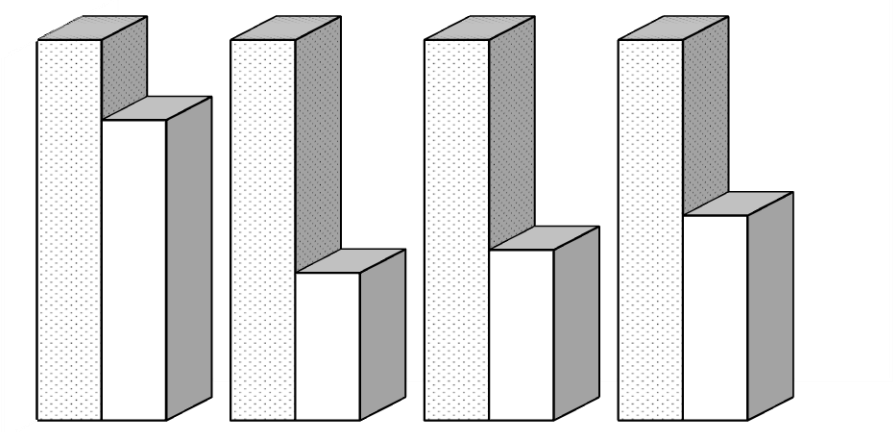

Fig. 1. Overall secretion of gastric juice and its basic components in dogs after combined effect of Enterosgel, ribotan and laser, 4 hours of experiment. 1- intact control, 2 experience, * P <0.05, ** P <0.01, *** P <0.001

Many authors point out exceptional role of hyperacidity in the pathogenesis of peptic ulcer disease (Geller PI, Geller, AP, 1989; Loginov AS, Aruin LI, Ilchenko AA, 1993; Lea Yu J., 1987; 1996; Ohlobystin AV 1997; Ohlobystin AV, Sheptulin AA, 1998), but there are no data on the effect of experimental gastric ulcer in secretory function of dogs in the literature. Therefore, one of the objectives of our study was to investigate the influence of experimental gastric ulcer on the secretory function of gastric glands.

We have found that the gastric mucosal damage caused changes in the secretory function of the gastric glands, accompanied by an increase in both volume of juice secreted and increasing concentrations of its major components.

The next stage of our study was to investigate the effects of Enterosgel on secretory function of gastric glands in experimental peptic ulcer. Figure 9 shows that over the four hours juice secretion decreased by 48%, free hydrochloric acid - by 61%, the total amount of acid and pepsin – by 54% - 56%. From the analysis it follows that Enterosgel is not only powerful enterosorbent, but it also has depressing effect on gastric secretory elements, and in particular on the principal and parietal gland cells.

In studying effect of ribotan on the secretory function of gastric glands in animals with peptic ulcer it was detected that over 4 hours juice secretion decreased by 4%, free hydrochloric acid - by 6%, the total amount of acids and pepsin - 4% and 4%. From this it follows that ribotan has no significant inhibitory action on gastric secretory elements, and in particular to the main cells and parietal glands.

In recent years, a model of physical therapy laser devices in combination with constant magnetic field was developed, the effect of which significantly increases permeability of quantum beam deep into the tissue. This combination provides high anti-edematous, reparative effect, including peptic ulcer disease, and is able to recover motor activity of the stomach in a short time in the postoperative period (Kalinin AV, 1996; Brill GE, 1997, Shevchenko AS ., Kobyalko VO, Ivanov VL, 1997). PMS itself is capable of reducing histamine content in the blood and nervous tissue (Rodin Yu, 1997; Gorbachev OJ, 2001). Given that histamine stimulates secretion of the parietal cells (Glinska NY, 1984; Green DM, Bishop AE, Rindi G. et al., 1989; Hakanson R, Chen D, Tielemans Y. et al., 1994), we assumed that its decrease in the body should alter functional activity of these cells and thus concentration of free hydrochloric acid in the gastric juice. Our study has shown that over 4 hours of experience juice secretion decreased by 33%, free hydrochloric acid - by 41%, total amount of acid - by 36% and pepsin - 40%. Thus, laser inhibits

secretory function of the main and parietal cells of gastric ulcer. Concentration of the components of the total juice secretion significantly reduced in relation to the benchmarks by reducing juice amount. As we pointed out, impact of laser on reduction of secretory function of gastric glands is the most pronounced after feeding, that is, during development of the food drive.

The next stage of our study was to investigate the influence of combined Enterosgel, ribotan and laser on secretory function of gastric glands in experimental ulcer disease. The main prerequisite for this was not only a selection of more effective treatment of peptic ulcer disease, but also the search for new ways to treat gastric secretory function. According to information from the scientific literature, whether low-intensity, used in peptic ulcer of the stomach and intestines, showed to be an effective method of treatment (Lutai AV, Egorova LA, MI Rasulov, 1996, Fedorova TA, 1997 ; Shutemova EA, 2001), has not only antispasmodic, anti-inflammatory properties, but also helps to reduce the aggressiveness of gastric juice (RO Bogachev, 1996).

Enterosgel has a high bio- and hemocompatibility, plasticity in the use does not damage the mucous membrane of the gastro - intestinal tract (even has the ability to enhance the regeneration of the epithelium) does not violate the membrane digestion easily (7-8 hours) is derived from the intestines. On the other hand, its ability to form hydrogels in aqueous phase (such as those as in the gastro-intestinal mucus glycoproteins) can impart enterosgel extremely important cytoprotective properties which provide enveloping effect on the mucosal surface of the stomach and intestine, preventing the cell from the external surface ¬nih mechanical and chemical aggressions, protecting it when ero¬ziyah and ulcerative processes (Mamaev IA, et al., 2000).

The results of using immunomodulators mixed. Most of the authors argue that immunokorektory contribute to a more rapid relief of subjective symptoms of the disease, early maturity scarring of the ulcer a long and stable remission (ES Golovanov, JN Romanova, 1988; Ilchenko AA, 1994). However, exposure to immunomodulators and their combined use in the secretory function of the stomach with ulcers in the literature are not illuminated.

Studies have shown that the combined effect Enterosgel, ribotan whether in SMS normalizes the secretory function of gastric glands, it happens both by reducing the volume of juice secreted, and due to the decrease in its concentration of its main components (Fig. 2).

The lymphatic system is actively involved in various pathological processes: the shock of various etiologies, inflammation, allergic, as well as the restructuring of the adaptation of the organism. Thus in the early stages of the lymphatic system are shown functional and morphological characteristics of the processes of damage, protection and accessories (YI Borodin 1997; YI Borodin, Lyubarskii Mikhail Efremov, AV et al., 1997).

Analyzing the results, it can be assumed that the high bulk density of the interstitial spaces in the lamina propria of the stomach indicates the overflow sections of the lymphatic system and violation of lymph flow, as in the presence of the ulcer occurs blockage of the lymph nodes or vessels tissue detritus coming in the inflammation that accompanies ulcerative process.

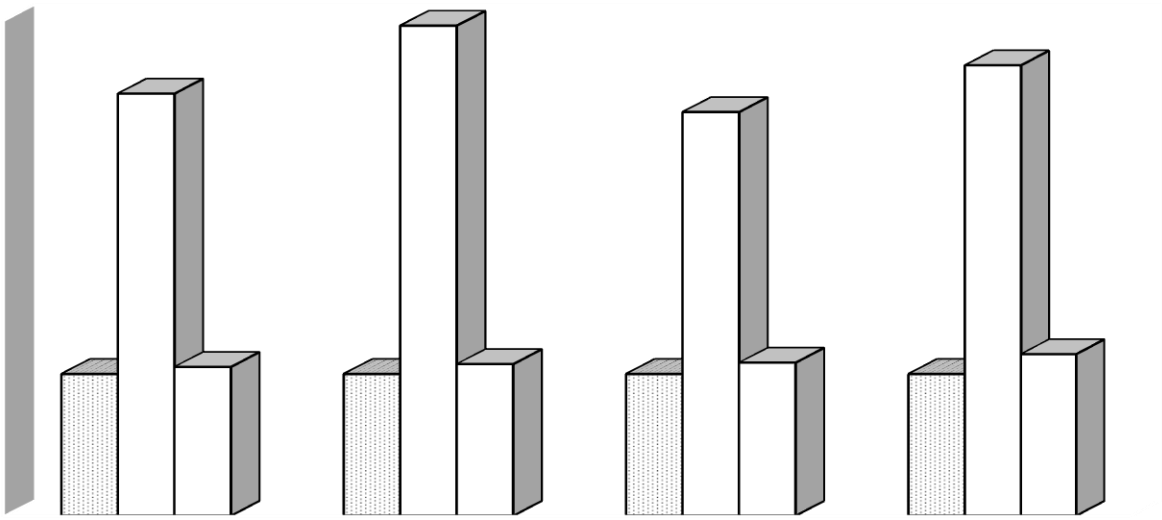

Fig. 2. The concentration of the main components of gastric juice in dogs for the treatment of gastric ulcer: 1- control; 2 - control; 3-experience. * P <0.05, ** P <0.01, *** P <0.001

The resulting studies lamina propria of the gastric mucosa after exposure enterosgelem data indicate that the bulk density of capillaries in the area of the cut, the bulk density of the lymph capillaries, the density of the interstitial spaces, the bulk density of cells and the intercellular substances ratio of cut blood vessels and cut area of interstitial spaces, the ratio of cut area to the area of the lymph vessels cutoff interstitial spaces in the course of treatment were not significantly changed.

By studying the histological findings in experimental animals after exposure ribotana can specify that the bulk density of capillaries in the area of the cut lamina propria, the ratio of the arteries and veins, the bulk density of the lymph capillaries, the density of the interstitial spaces, interstitial spaces, bulk density of cells and intercellular substance, the ratio of cutting blood vessels and interstitial spaces of the square cut, the ratio of the area of the cut lymphatic vessels had no significant differences. A ratio of cut blood vessels and interstitial spaces to the area of the cells and the intercellular substance in the course of therapy ribotanom had significant differences. According to a biopsy of the control group, the figure was in the range of 0.310 to 0.560. During treatment, the lower limit of a number of variations was equal to 0.125, and the top 0,134, and, in 72% of dogs, this figure was lower than 0.123.

Histological data group of animals on the background of the impact of laser radiation in a constant magnetic field indicate that the bulk density of capillaries in the area of the cut lamina propria has no significant changes in the ratio of arteries and veins also did not differ significantly. Bulk density of the lymph capillaries, the density of the interstitial spaces in the lamina propria, also had no significant differences, but there was a slight tendency to increase them. Bulk density of cells and intercellular substance on the cut lamina propria in this group during the treatment did not have significant differences, but there was a slight tendency to decrease. The ratio of cut blood vessels and interstitial spaces of the square cut, the ratio of the area of the cut lymphatic vessels to the area cut the interstitial spaces of the control group and the therapy did not significantly differ. The ratio of cut blood vessels and interstitial spaces to the area of cells and the intercellular substances during laser treatment was carried out significant differences. The treatment laser radiation in the SRL, the lower limit of a number of variations was equal to 0.128, 0.136 and the upper, and, in 75% of dogs, this figure was lower than 0.128.

As a result of the impact of separate series of experiments enterosgelya, ribotana and laser radiation in the SRL can speak with confidence about their different effects on the microcirculation of the lamina propria in experimental gastric ulcer. Therefore, our next task was to study the simultaneous (combined) effects of test factors, as we have suggested that this combination can cause a qualitatively different response of the local blood flow. The scientific literature on the subject of information we found.

By analyzing the data obtained in the study of biopsy material in experimental animals treated with combined therapy of peptic ulcer immunomodulatory drug ribotan, enterosgelem, in conjunction with the laser in a constant magnetic field, we can say the following: The bulk density of capillaries in the area of the cut lamina propria was 5.81% number of arteries vary significantly compared with the control, the bulk density of lymphatic capillaries was significantly increased (40%). There was a significant difference between the density of interstitial spaces on the cut lamina propria during treatment. The ratio of the cut lymphatic vessels to the area cut interstitial spaces during treatment had significant difference, and ranged from 0.220 to 0.241 (Table 1).

Thus, against the background of complex treatment stoped signs of inflammation, improves microcirculation, lymph flow, and thereby reduces the number of interstitial spaces. In connection with the restoration of the drainage function of the lymphatic system, improving lymph flow, treatment of inflammation (swelling) decreases and the area of the cut lymphatic vessels, and thereby increasing their number, enters the field of view.

Table 1. Structural organization lamina propria background of complex treatment of experimental gastric ulcer ribotanom, enterosgelem in conjunction with the laser in a constant magnetic field (M ± m)

Исследуемый параметр	контрольная	опытная
Артерии	3,600 ±0,350	2,930 ±0,100*
Вены	2,501 ±0,320	2,880 ±0,120
Лимфатические сосуды	2,431 ±0,340	3,641 ±0,130*
Интерстициальные пространства	22,110 ± 0,810	15,720 ±0,710*
Клетки и межклеточное вещество	69,990 ±2,810	71, 320 ±2,680
Отношение площади среза кровеносных сосудов к площади среза интерстициальных пространств	0,276 ± 0,084	0,369 ± 0,040
Отношение площади среза лимфатических сосудов к площади среза интерстициальных пространств	0,109 ±0,031	0,231 ±0,011*
Отношение площади среза сосудов и интерстициальных пространств к площади среза клеток и межклеточного вещества	0,436 ±0,122	0,352 ±0,081

Note: * - significant difference between the values of variables between the groups. The research results are presented in the bulk density of the structures (the percentage of the area of the cut zone).

Identified in our study of the structural features of the reactions of the lamina propria of the gastric mucosa of dogs in experimental ulcer disease confirm the validity of scientific views on the development of a chronic process. Cellular composition of the lamina propria of the gastric mucosa of dogs with experimental ulcer we noted that numerical density and absolute number of leukocytes in tissue mucosa at the beginning of the experiment was significantly greater than at its end. V.V.Serov, AB Schechter (1981) consider that the expression signs of chronic inflammation is to reduce the number of neutrophils with an increase in the number of lymphocytes, monocytes and macrophages. According to some scholars (Schechter AB Aruin LI Gorodinskaya BC, Milovanova ZP, 1993; Aruin LI and Soave .. 1998), this morphological pattern characteristic of more mature chronic process, a decrease vascular permeability and increase in neutrophil migration of lymphocytes and monocytes.

Enterosgel is a sorbent that actively binds toxic metabolites, but its impact on the structural changes in the inflammation remains unexplored. In the study of tissue leukocytes in the lamina propria of the gastric mucosa in dogs with a peptic ulcer during treatment enterosgelem we note that the number density of white blood cells is reduced by 1.8 times. The relative number of neutrophils, eosinophils and plasma cells degenerating have a clear tendency to a decrease in biopsy also noted a decrease in the relative number of red blood cells. These changes histology we associated with a decrease in the permeability of the walls of both microvascular and by enveloping action and neutralize the stimulus (hydrochloric acid).

Immunological disorders characteristic of many diseases of the digestive system, including for gastric ulcer (Bondarchuk GF 1982; Burlakov EB 1976; Kryshen ZP, Shamshonkova TP 1982; Loginov .With., Tsaregorodtseva TM Zstina MM, 1986). However, available data in the literature describing the role of the immune system during chronic peptic ulcer contradictory (IF Karpov, 1983). Data on targeted imunokorrektsii ulcer disease are rare and concern only the specific immunomodulators (A. Leonov, 1986; Tarasova GN 1989; Ilchenko, AA, 1994), the results of the application, according to various authors are ambiguous. Most reports emphasized that immunomodulators contribute to a more rapid relief of subjective symptoms of the disease, early maturity scarring of the ulcer, a long and sustained remission (Zemskov VM, Perederiy VG, 1984; Rustamov SB 1987). These messages coincide with the results of our research.

The numerical density of tissue leukocytes in the lamina propria of the gastric mucosa in dogs during treatment ribotanom decreased by 1.9 times. Ratios of lymphocytes, neutrophils, and plasma degenerating cells and erythrocytes immunokorregirujushchej background therapy tends to decrease and are not significant.

The relative index of eosinophils, mast cells, monocytes, macrophages increased significantly. Macrophages - the permanent members of the immune response. Furthermore, these cells secrete large amounts of enzymes, cytokines, and other substances into the surrounding tissue, and secretion depend on their activity. Macrophage cytokines increase the intensity of DNA synthesis in lymphocytes, accelerate the maturation of thymocytes to T-cells. They accelerate the differentiation of B lymphocytes into plasma cells. Macrophage system is highly mobile system and interacting with lymphocytes with them is a functional unit (Aliev AA, 1985; Aruin LI 1998). These cells are a major source of chemical mediators of inflammation, cause proliferation and maturation of fibroblasts and formation of connective tissue. (Michel L. et al., 1992; B. Ruger et al., 1994). Consequently ribotan stimulates these cells, which accelerates the healing of the ulcer.

Several authors have noted anti-inflammatory and reparative effect of magnetic-laser therapy for stomach ulcers (VE Illarionov, 1992; L. Barsukov, 1994; Maksimenko TA Korotych OP, RP Stepanenko, 1994) .

In our studies, numerical density of tissue leukocytes in the lamina propria of the gastric mucosa in dogs during treatment with the laser in a constant magnetic field is reduced to 1.98 times. Ratios of lymphocytes, neutrophils, and plasma degenerating cells and erythrocytes against laser treatment tended to decrease. Therefore laser treatment reduces the activity of the inflammatory response and is accompanied by a decrease in the number of lymphoid plasma cells that is consistent with the opinion of some authors (Mikhail Khutsishvili, 1990; ND Pletnev, 1991).

The relative index of eosinophils, mast cells, monocytes, macrophages increased significantly. At congenial number of these cells increases dramatically as in the pathological focus, and in the surrounding tissues (Aruin LI 1986; VH Vasilenko, 1987). This histological picture is viewed as a positive effect of laser and magnetic therapy in the treatment of experimental gastric ulcer.

Cytogram tissue leukocytes gastric mucosa of dogs in experimental ulcer disease on the background of combined treatment enterosgelem, ribotanom and laser radiation is characterized by a decrease in the SMS number of white blood cells by 42%, their absolute index ranged from 5.44 to 7.02 cells per 105 mm2.

The absolute number of lymphocytes index ranged from 1,830 to 2,864 by 105 mm2; neutrophils from 1,830 to 2,864; eosinophils from 0.085 to 0.167; erythrocytes from 0, 249 to 0,353, from 0,052 obese to 0.156; plasma from 0.022 to 0.138, degenerating cells from 0.058 to 0.208, accounting for 25%, 20%, 4%, 20%, 48%, 6%, respectively. Absolute figures the number of monocytes in the lamina propria accompanied by an increase, and ranged from 0.861 to 1.02 for 105 mm2, macrophages from 0.44 to 0.208, which amounted to 20% and 55%, respectively (Table 2).

Studies have shown that combination therapy with gastric ulcer does possess anti-inflammatory and reparative effects, manifested by decreased activity of the inflammatory response to a decrease in the number of lymphoid plasma cells.

Table 2. The cellular composition of the gastric mucosa in dogs in the background combined treatment enterosgelem, ribotanom and laser radiation in the SRL experimental ulcer disease (M ± m).

Исследуемый параметр		контрольная	опытная
Численная плотность лейкоцитов	NA	10,70 ± 0,26	6,26 ± 0,82*
Лимфоциты	%	46,20 ± 3,97	39,92 ± 2,71
	NA	2,520 ±0,158	1,924 ± 0,094*
Нейтрофилы	%	23,69 ± 1,82	18,96 ± 1,76*
	NA	1,197 ± 0,145	0,904 ± 0,516
Эозинофилы	%	5,89 ± 1,31	4,12 ± 0,85
	NA	0,187 ± 0,077	0,126 ± 0,041

Тучные клетки	%	3,69 ± 1,17	1,92 ± 1,06
	NA	0,119 ± 0,064	0,104 ± 0,052
Эритроциты	%	7,20 ± 0,34	5,88 ± 0,62*
	NA	0,271 ± 0,092	0,181 ± 0,052
Моноциты	%	4,80 ± 1,41	19,12 ± 2,07*
	NA	0,154 ± 0,087	0,942 ± 0,081*
Макрофаги	%	2,40 ± 0,751	5,32 ± 1,27*
	NA	0,118 ± 0,125	0,176 ± 0,032
Дегенерирующие клетки	%	5,02 ± 1,02	1,40 ± 0,17*
	NA	0,168 ±0,092	0,098 ±0,004
Плазматические клетки	%	3,50 ±1,202	2,25 ±1,06
	NA	0,131 ±0,084	0,106 ±0,084

Note: NA- numerical cell density of 105 square meters. micron cutoff zone; * - Significant difference between the values of variables between the groups.

It is known that neutrophil granulocytes play an important role in all stages of the development of peptic ulcer disease and is closely associated with many of its manifestations. These cells are the first to appear at the site of damaged tissues. Neutrophils are capable of migration, phagocytosis is performed and secrete lysosomal enzymes and various mediators, which increase vascular permeability, activate T-lymphocytes and macrophages. Extravascular migration and accumulation of neutrophils at the site of damage and penetration of antigens - one of the main manifestations of the cellular immune response. Abundant tissue infiltration of neutrophils in conjunction with impaired microcirculation causes malnutrition tissues (Aruin LI 1986; Aruin LI 1998).

Lymphocytes - immunocompetent cells that interact with other cells, is carried out protection of an organism and quantitative characterization of lymphocytes in the immune process in the inflammatory infiltrate and has not only theoretical interest, but also a certain diagnostic and prognostic importance (Abdullayev J. C., 1999; A Aruin .i., 1998).

A large number of eosinophils in the tissue should always be considered from the standpoint of the possible activation of mast cells, which are precursors of immediate allergic reaction. Apparently, eosinophils bind histamine released by mast cells. It is shown that their effector function, eosinophils operate in immune inflammation foci. In addition, clinical and laboratory data shows that some of the products of secretion of these cells can cause damage to the endothelium, thrombus formation and impaired microcirculation (Aruin LI 1986; Aruin LI 1998; VH Vasilenko, 1987) .

Mast cells are a major source of chemical mediators of inflammation. If the damage of the stomach epithelium, tissues and cells of the body are subjected to dystrophic changes right up to necrosis. The

decay products of cells and tissues, lysosomal enzymes and chemical mediators from macrophages and neutrophils lead to the expansion of the blood level of the microvasculature and on to the arterial and venous congestion, slowing blood flow, stasis, thrombosis or hemorrhage (Aliev AA, 1985; L. Aruin I., 1998). The first of the vessels are located in the tissue neutrophils in severe lesions of the endothelium appears diapedesis of red blood cells. Somewhat later, the hearth of the pathological process is filled monocytes, lymphocytes and macrophages.

It should be noted that most of the cells in inflammatory and immune reactions comes from the blood flow, but may migrate to the site of the antigen and the appearance of tissue macrophages (resident) macrophages of surrounding tissues. Moreover, the dynamics of macrophage reaction associated with the passage of the pathological process. Occurring degenerating cells may result from imperfect proliferation, resulting in rapid apoptosis, and can also indicate increasing cellular immunity and enhance the regeneration of damaged tissue (lysis destroyed tissues more appearance of fibroblasts and replacement with scar tissue ulcer).

Thus, scarring ulcer amid combined treatment is accompanied by a decrease in the number of lymphocytes, neutrophils, erythrocytes, mast, plasma, degenerating cells and increased number of eosinophils, monocytes and macrophages in the lamina propria edge ulcers.

One of the objectives of our work was to study the separate and combined influence enterosgelya, ribotana and laser radiation in the SRL on the morphofunctional state periultseroznogo infiltrate, ulcer and stomach wall. For its successful solutions we have used experimental animals mortem autopsy, histological and morphometric study of the ulcer and periultseroznogo infiltration of the gastric mucosa. In the macroscopic study, we took into account the location, shape, size and stage of development of the ulcer, the presence of periultseroznogo infiltrate the state of the gastric mucosa. All experimental animals at the border of the lower third of the stomach and pyloric found chronic ulcer. The untreated group of dogs macroscopic changes were located only in the area of the ulcer were almost similar. The difference lies in the reduction of the area of the ulcer of the stomach wall by 35.3% ($P < 0.01$) and periultseroznogo infiltration by 12.1% ($P > 0.05$). This fact can be considered as stable inflammation and ulcers in the pereultseroznoy zone. In groups of dogs with various treatments macroscopic changes were characterized by healing process of gastric ulcers. What manifested significant decrease in the area of the ulcer, periultseroznogo infiltration and cleansing of the ulcer of fibrin and necrotic masses. Of all the ways to treat the best therapeutic effect as reaching the stage of pink scar was observed with concomitant use enterosgelya, ribotana and laser in SMS within 14 days. After studying the macroscopic picture of chronic ulcers examined histologically state of the ulcer. In this area, it was necessary to study the structure of the bottom and the edges of ulcers, because according to LI Aruin (1998), II Degtyareva (1995) and others. Detritus severity zone in the bottom of the ulcer may be considered as the activity index of the ulcer and sloughing and epithelization along the edges of the ulcer index as the start repair. The formation and maturation of the granulation tissue at the bottom and the edges of the ulcer suggests the creation of favorable conditions for the healing of the ulcer (Serov VV, 1995). The obtained histopathological evidence suggests that all experimental animals in the wall of the stomach ulcer was detected single microscopic representation of a typical ulcerative defect, polymorphonuclear cell infiltration, granulation tissue filling the edges and bottom of the ulcer.

Animals without treatment on the eighth day granulation tissue was characterized as a young and by 22 days it took on a more mature form of a decrease in vascular permeability for neutrophils and increased migration of lymphocytes and monocytes, which explained the characteristic of chronic inflammation of the change in the endothelial adhesion molecules E-selectin on VCAM -1. According to some scientists (Serov VV, VS Spiders, 1995; Myagkova LP Sklyansky TL, MY Lapin, et al., 1997; Aruin LI and Soave. 1998) received a microscopic picture is confirmed by the development of chronic ulcers. Smears of stomach ulcers in dogs treatment groups in the dynamics of cleansing the ulcer was characterized by detritus, decreasing edema and inflammatory infiltration, maturation and transformation of fibrous scar tissue

granulation and epithelization ulcer. Optimal results reparative regeneration was observed with concomitant use ribotana, enterosgelya and laser PMP. Dogs in this group, unlike other groups, after fourteen days of treatment the ulcer heal by secondary intention by means of granulation tissue, which corresponds to the phenomenon of substitution. This result is in our opinion is good, despite the fact that the optimal outcome of any reparative regeneration is restitution. Since according to LI Aruin (1998), MM Boger (1986) all ulcers heal by secondary intention by means of granulation tissue. After histological study of the ulcer was necessary to explore periultserozny infiltrate due to the fact that he is not only a consequence of the ulcer, but also plays an important role in the healing and ulcer recurrence. Periultseroznaya zone in the experimental groups throughout the experiment was characterized by infiltration of polymorphonuclear leukocytes epithelium and lamina propria on the background of infiltration by lymphocytes and plasma cells, which can be regarded as a local active chronic gastritis with different stages of activity. The level of activity found out by means of morphometric analysis of the inflammatory infiltrate in the mucosa pereultseroznoy zone. Morphometric we have not found significant differences between indicators of nuclear-cytoplasmic ratio in the cover-pit epithelium and the number of plasma cells in all groups. Other indicators pereultseroznoy area had a variety of changes. In dogs, without treatment with increasing duration of chronic stomach ulcers and 22 days severity of infiltration of the epithelium and lamina propria did not undergo significant changes. Most significantly changed the volume fraction of polymorphonuclear leukocytes in the direction of reducing by 47% ($P < 0.05$) and an increase in the volume fraction of macrophages by 45% ($P < 0.05$), lymphocytes by 12% ($P < 0.05$). These changes were due to chronicity of inflammatory process in the ulcer. In groups of dogs with a variety of treatments was observed a significant decrease in lymphoplasmacytic and polymorphonuclear infiltration periultseroznoy area inversely proportional to the duration of the treatment of chronic ulcers. In dogs with concomitant use of enterosgelya, ribotana and laser PMP mucosa periultseroznoy area it did not differ from the mucous membrane of intact animals. The only difference noted the presence of individual fibroblasts ($0.2 \pm 0.03\%$ ($P < 0.001$)) and a significant increase in the volume fraction of macrophages by 1.16% ($P < 0.05$). In other experimental groups indicators periultseroznogo infiltrate mucosa were significantly higher than those in the intact control, but compared to the group without treatment and neutrophilic infiltration monuklearnaya had significantly lower performance. Consequently, the absence of leukocyte infiltration of the gastric mucosa periultseroznoy area with combination of enterosgelya, ribotana and laser PMP is an additional argument, speaking about the full and adequate treatment. Since the recurrence of peptic ulcer disease occurs earlier in the presence of residual inflammatory changes of the mucous membrane around the ulcer after scarring (Degtyareva II, NV Harchenko, 1995).

conclusions

1. In the experimental peptic ulcer increases the secretory function of gastric glands, which manifests an increase in the volume of juice secreted by 138%, increasing the concentration of the main components of it: free hydrochloric acid at 246%, the total amount of 185% acid and pepsin by 218%.

2. Enterosgel inhibits the function of the secretory elements lining the stomach cancer. This occurs both by reducing juice secretion by 36% and by reducing the concentration of its basic components: free hydrochloric acid at 79%, the total amount of acid of 68% and 63% pepsin. Ribotan does not change the secretory function of the main and parietal cells. With an overall downward trend in the concentration of components of juice, the secretion of their total does not differ from the benchmark. After the laser irradiation in a constant magnetic field, the concentration of the components of gastric juice has a tendency to decrease, but their total secretion increases: free hydrochloric acid at 23%, the total amount of acid by 57% and pepsin by 48% due to increased volume of juice to 55%.

3. The combined impact enterosgelya, ribotana and laser in a constant magnetic field inhibits the secretion of gastric glands throughout the observation. Thus there is a decrease in the volume of juice to 21%, and the concentration of its basic components: free hydrochloric acid at 61%, the total amount of acid of 55% and 46% pepsin.

4. In the experimental gastric ulcer enterosgel depressing effect on gastric secretory elements: juice secretion decreased by 48%, free hydrochloric acid at 61%, the total amount of acid by 54% and 56% pepsin. Ribotan in experimental gastric ulcer does not change the secretory function of the main and parietal cells. With an overall downward trend in the concentration of the components of the total juice secretion had no statistically significant difference from the benchmarks. Laser radiation in a constant magnetic field with experimental gastric ulcer inhibits the secretory function of the main and parietal cells of the gastric glands. Gastric acid secretion reduced by 33% free hydrochloric acid at 41%, the total amount of acid is 36%, and 40% pepsin.

5. The combined effect of enterosgelya, ribotana and laser in a constant magnetic field normalizes the secretory function of the gland in experimental gastric ulcer, which occurs as a by reducing the volume of juice secreted by 133%, and due to the decrease in its concentration of its main components: free hydrochloric acid to 239%, the total amount of 177% acid and pepsin by 204%.

6. Combined treatment of experimental gastric ulcer ribotanom, enterosgelem and laser in a constant magnetic field improves microcirculation and lymphatic flow of the gastric mucosa, as evidenced by an increase in bulk density of lymphatic capillaries in the area of the cut lamina propria by 33%, ratio of the area to cut lymphatic vessels Square cut the interstitial spaces by 53%, reduction in the density of the interstitial spaces by 29%.

7. The developed method of combined use of anti-ulcer therapy using enterosgelya, ribotana and laser light in a static magnetic field reduces the acute inflammatory response in the edges of the ulcer, as evidenced by reduction in the number of lymphocytes by 25% and 20% of neutrophils, eosinophils, 4%, red cells 20%, fat 48%, 36% plasma, degenerating cells and 6% increase in the number of monocytes by 20%, 55% macrophages.

8. On gross examination of the stomach in the group with the combined use of enterosgelya, ribotana and laser in a constant magnetic field on the 14th day watching the healing of gastric ulcers with the achievement stage of pink scar.

9. The combined application enterosgelya, ribotana and laser in a constant magnetic field on the 14th day in the gastric mucosa of gastritis periultseroznogo phenomenon is not determined, as evidenced by the absence of polymorphocellular, limfoplazmatsitarnoy infiltration, the presence of isolated fibroblasts and macrophages.

Practical suggestions

These peculiarities of the clinical status and histomorphological manifestations of chronic stomach ulcers deepen and broaden scientific understanding of the dynamics of structural changes in the wall of the stomach with ulcers.

The data obtained can be used:

-in the educational process for the lectures and workshops on the veterinary faculties of higher education, faculty training, etc .;

- In the writing of the relevant sections and manuals on non-contagious disease of the gastrointestinal tract;

- In practice, the improvement of clinical and morphological diagnosis of gastric ulcer.

The proposed complex therapy includes:

1. Exposure of the stomach laser in a constant magnetic field of the four zones of 2 minutes each at 50 Hz and power 40-45MVt within 14 days

2. Orally administered enterosgel dose of 0.2 grams per kilogram of body weight for 14 days.

3. Intramuscular ribotana at a dose of 1.0 ml per 10 kg of body weight every other day for 14 days.

It can be used as an independent method of treatment for stomach ulcers in dogs.

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List of abbreviations

..... GI gastrointestinal tract

MEL ....mezhepitelialnye lymphocytes

H * ....iony hydrogen

H20 Water .....

HP ....Helicobacter pylori

HCl hydrochloric acid ....

FGS ....fibrogastroskopiya

BU ..... .yazvennaya disease

DU ..... duodenal ulcer

GU ....yazvennaya stomach trouble

EYABZH .... experimental gastric ulcer

CO ..... .slizistaya shell

Coolant ..... .slizistaya stomach lining

THERE ....lazernoe radiation

PMP ....postoyannoe magnetic field

LLLT laser light ..... nizkoentensivnoe

PAUL .... lipid peroxidation