ORIGINAL ARTICLE

Application of mineral waters in the complex treatment of patients with gastroesophageal reflux disease

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ABSTRACT

BACKGROUND: Gastroesophageal reflux disease (GERD) is one of the most common gastric pathologies. Recently, there has been a growing interest in the healing effects of mineral waters (MW).
METHODS: Ninety patients with GERD were under observation. The study used the following methods: anamnestic, clinical, studies of biochemical blood parameters, ultrasonographic studies of the digestive system, fibroesophagogastroduodenoscopy with intragastric pH-metric. After preliminary research, all patients were randomly divided into three groups of 30 people. The control group (group 1) who were prescribed a basic treatment complex-dietary and proton pump inhibitor group drugs. Patients of group 2 in addition to the standard course of treatment received boric highly mineralized bicarbonate sodium water. Patients of group 3 in addition to the basic therapy were prescribed an internal course treatment of highly mineralized sulfate-bicarbonate sodium-magnesium water.
RESULTS: The use of the basic complex of treatment for a month in control group did not lead to a significant leveling of signs of dyspeptic and asthenic syndromes. The use of boron highly mineralized sodium bicarbonate water led to a significant leveling of signs of abdominal pain and dyspeptic syndromes, improvement of acid-forming function of the stomach, but no reliable dynamics were observed in eliminating signs of cytolytic, mesenchymal inflammatory and cholestatic syndromes. Application of highly mineralized sulfate-hydrocarbonate sodium magnesium water improves the elimination of dyspepsia and pain syndromes, normalization of the functional state of the liver.
CONCLUSIONS: The obtained data confirm the prospects of using highly mineralized mineral waters in the complex treatment of GERD patients.

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There are many definitions of gastroesophageal reflux disease (GERD), but their common essence is defined in the recommendations of the Montreal Consensus in 2006, where GERD is defined as a condition that develops when the reflux of the stomach contents causes "alarming"

symptoms and/or complications.[1, 2] Currently, GERD is one of the most common pathologies in the structure of acid-related diseases. The incidence of GERD in the world is 5 per 1 thousand people per year.[3, 4] In Europe and the United States, the disease is diagnosed in 10-40% of the adult population and this upward trend is constantly increasing.[5-8] There are two main forms of GERD: non-erosive reflux disease (NERD) and erosive esophagitis.

The Montreal Classification presents a division of the manifestations of GERD into esophageal and extraesophageal, as well as the degree of interrelation of associated states and GERD. Treat esophageal syndromes: symptomatic (classical reflux syndrome, chest pain syndrome associated with reflux) and syndromes indicating damage to the esophagus (reflux esophagitis, reflux stricture, Barrett's esophagus, esophageal adenocarcinoma). Extraesophageal syndromes include syndromes with proven causal connection with reflux: cough syndrome, laryngitis, asthma, dental erosion. As well as syndromes that have a probable association: pharyngitis, sinusitis, recurrent inflammation of the middle ear.[9]

Heartburn is considered one of the most characteristic symptoms of this disease. In the mechanism of its development, there is pathological gastroesophageal reflux (GER), which is a high frequency and/or duration of episodes of throwing acidic contents of the stomach into the esophagus.[10] This contributes to dysfunction of the lower esophageal sphincter (failure of the locking mechanism of the cardia), caused by the primary decrease in pressure in the lower esophageal sphincter (LES), as well as hernias of the esophagus aperture of the diaphragm (HEAD), which leads to an increase in the number of episodes of transient relaxation for its full or partial destructuring.

The development of HEAD disrupts the functioning of the antireflux mechanism. The frequency of detecting HEAD in the population ranges from 3% to 33%, and in the elderly, it reaches 50%. In general, a decrease in LES tone and an increase in cases of an insufficient obstructive function of LES are detected in 80% of patients with GERD. However, the mechanisms of their occurrence in the pathogenesis of GERD

are not well understood.[11, 12] The appearance of GER is promoted by various factors leading to an increase in intra-abdominal and intra-gastric pressure. It has been proven that the severity of the inflammatory process in the mucous membrane of the esophagus in patients with erosive GERD correlates with markers of obesity, both visceral and general.

Among other risk factors for GERD, there is a sufficient list of drugs that can provoke and aggravate gastroesophageal reflux. Among these drugs, which are most often taken by elderly patients, antispasmodics, β-blockers, sedatives and hypnotics (especially benzodiazepines), nitrates, theophylline, calcium antagonists and nonsteroidal anti-inflammatory drugs are particularly dangerous.[13, 14] One of the mechanisms for the occurrence of postprandial reflux and heartburn is a violation of the motor function of the stomach, resulting in the formation of a layer ("pond") of the acid immediately near the cardia, called the "acid pocket". After eating, the buffer properties of food should reduce the acidity of gastric contents. The paradox is that the upper part of the chyme in the area of the bottom of the stomach has a pH value of 1.6-1.7 units, pH, that is, corresponding to high acidity, and the contents of the stomach in the distal part has a pH>4.4 units, pH, indicating a lower acidity of chyme. The postprandial "acid pocket" can persist for 2 hours after a meal, being a reservoir for acid GER in both healthy people and GERD patients. However, in patients with GERD, the "acid pocket" is enlarged and may be located above the diaphragm due to the HEO, which increases the severity of gastroesophageal reflux.

Under the influence of the pathological GER the esophagus may cause a variety of symptoms and lesions of symptoms and damage may occur (esophagitis, erosion, and strictures of the esophagus, Barrett's esophagus, adenocarcinoma of the esophagus), which depend on:

• the composition of refluxate (hydrochloric acid, pepsin, bile acids, lysocetin, pancreatic enzymes);

• the duration of the effects of reflux on the esophagus;

• state of resistance of the esophageal mucosa. Reduced resistance of the esophageal mucosa

is associated with reactions of oxidative stress in the distal esophagus with increased inactivation of nitric oxide and a decrease in its cytoprotective effect on the esophageal mucosa, which contributes to the suppression of anti-inflammatory cytokines, enhances apoptosis, and ultimately leads to the development of inflammation in its mucosa shell.[15] The proven relationship in the violation of the metabolism of nitric oxide with the formation of gastroesophageal refluxes in patients with a combined course of GERD and hypertension.[16]

In patients with GERD over 60 years of age, arterial hypertension (58.9%) and coronary heart disease (41%) dominate in the structure of comorbidities, requiring constant use of appropriate drugs.

Increased acidity, bile acids of gastric contents and a long-term "acid pocket" lead not only to the development of heartburn but also to the appearance of dyspepsia symptoms, such as heaviness and pain in the epigastral region after eating, belching and bloating. Moreover, the characteristic complaint of functional dyspepsia to epigastric severity after eating is found in patients with GERD even more often than its classic symptom, heartburn.

For many patients, dyspepsia and GER are interrelated.[17, 18] As part of a multicenter study of MEGRE,[19] a higher incidence of concomitant symptoms of functional dyspepsia (FD) due to impaired kinetic properties of the upper gastrointestinal tract in the group of patients with GERD was found compared with patients who did not meet the criteria for GERD. So, symptoms of FD (severity in the epigastric region after eating, belching, etc.) were observed in 70% of respondents with symptomatology of GERD and in 42% of respondents who did not fully meet the criteria for GERD. According to the survey, 55% of respondents had biliary system diseases, including 73% in the group of patients with GERD and 34% in the group without GERD. The authors analyzed the results of a survey of more than 1000 patients with symptoms of GERD and dyspepsia. It has been established that the crossover between GERD and FD reached 30-40%.

When examining 2388 patients Y.W. Noh *et al.*, Showed that signs of FD were found in both patients with GERD and patients with NERD. At the same time, cross-symptoms were more common in patients with NERD than in patients with reflux esophagitis, respectively, 74.3% and 10.5%.

In the analysis of literature on the prevalence of dyspeptic symptoms in patients with GERD (based on 2057 studies), the authors conclude that in patients with nonerosive GERD, there is a more frequent prevalence of dyspepsia symptoms and a weaker response to therapy with proton pump inhibitors (PPI) compared with patients with erosive esophagitis (level of evidence A).[20] In another large-scale study, a frequent combination of FD, GERD, and irritable bowel syndrome with a high prevalence of dyspepsia was detected.[6]

In patients younger than 60 years, GERD was found to be more often combined with hepatopancreatoduodenal diseases — chronic pancreatitis (34%), liver steatosis (22%), duodenal ulcer (19%), chronic cholecystitis (17%), which also may be accompanied by symptoms of dyspepsia.

Increased acidity of gastric contents and a long-existing "acid pocket" lead not only to the development of heartburn but also to the appearance of symptoms of dyspepsia. Such an overlap syndrome is due to the common pathogenetic mechanisms: the presence of an "acid pocket", an acid-peptic factor, a violation of the motor function of the upper gastrointestinal tract, visceral hypersensitivity and the psyche of the patient.[12]

Thus, the various dyspeptic symptoms observed in patients with GERD significantly reduce their health-related quality of life.

The basis of GERD therapy is the use of antisecretory drugs.[21] According to the Genvalsky consensus, the most modern and effective today are drugs of the proton pump inhibitor group (PPI), which are prescribed in standard doses. In the presence of stage "A" (Los Angeles Classification, 1994), a 4-week course of PPI (esomeprazole 40 mg, rabeprazole 20 mg, pantoprazole 40 mg, etc.) is recommended 30-60 minutes before breakfast. With multiple erosions of the esophagus (stage "B" and "D"), as well as with complications of GERD, the treatment lasts at least 8

weeks. At the same time, maintenance therapy in the future with the use of a standard or half-dose of PPI ensures remission in 80-90% of patients for 1 year.[22] On the contrary, with endoscopically negative GERD, which in the structure of GERD reaches 60-70%, a certain proportion of patients do not respond to therapy not only with standard but double doses of PPI. However, increasing the effectiveness of treatment of GERD with acid-suppressive drugs by increasing the dosage of the drug and the duration of therapy leads to the development of adverse events that are caused by prolonged acid suppression.[23] This is primarily a violation of the absorption of calcium, iron, zinc, impaired absorption of a number of drugs (L-thyroxin, theophylline, calcium carbonate, fluconazole, iron preparations), for the assimilation of which it is important to maintain physiological pH values. Due to prolonged acid suppression, the normal microflora of the stomach and intestines may change, infections of the respiratory tract and gastrointestinal tract may develop, the organism's immunological reactivity may be disturbed, and the risk of cancer may increase.

For a long time, the main reasons for the refractory course of GERD were: insufficient patient integrity in treatment (failure to eat and take PPI in a timely manner), the presence of "nightly acid breakouts," when the pH in the esophagus is <4 units. The pH is more than one hour at night and the ability of cytochrome P 450 to metabolize PPI.

Currently, according to a number of authors,[24, 25] it has been found that acid suppressive therapy does not eliminate the impaired motor-evacuation function of the organs of the esophagogastroduodenal and biliary systems, the hypersensitivity of the esophagus and the damaging, cytotoxic effect on the esophageal mucosa of refluxate components, which include bile acids (BA), lysolitsetin and pancreatic enzymes (trypsin and pancreatic phospholipase). It is established that when the pH of the esophagus is from 2.0 to 4.0 units aggressive properties, potentiated by the destructive action of hydrochloric acid, exhibit pepsin, lysole-acetin and lysolecithin-conjugated BA. At the same time, unconjugated and dihydroxylic acids, as well as trypsin, penetrating into the esophageal mucosa,

have a more pronounced damaging effect at neutral and weakly alkaline pH.[26, 27]

With mixed reflux, PPI therapy leads to the prevalence of unconjugated BA over conjugated, and long-term secretory therapy can lead to metaplasia and epithelial dysplasia.

It was established that pathological refluxate containing pepsin, trypsin, hydrochloric acid, has a stimulating effect on epithelial cells, which leads to the production of proinflammatory cytokines: IL-1 B, IL-6, IL-8 and IL-10.[28] The resulting chronic inflammation occurs with the involvement of fibroblasts, muscle, immune and endothelial cells in the pathological process, leading to fibrosis, aggravation of motor disorders of the esophagus and the formation of adenocarcinoma.

Thus, the composition of refluxate plays a role in the progression of GERD and the development of its complications (Barrett's esophagus and esophageal adenocarcinoma).[29]

Insufficient effectiveness of antisecretory drugs in patients with symptoms of GERD and functional dyspepsia is also associated with impaired cleansing ("clearance") of the esophagus from the aggressive components of refluxate, increasing the duration of its negative effect on the esophagus, increasing the number of transient relaxations of the lower esophageal sphincter. In addition, the PPIs themselves can weaken the motility of the stomach and slow its emptying.

Thus, at present, GERD should be considered as a disease with complex, multicomponent pathogenesis, which is often combined with multiple comorbidities (functional dyspepsia, obesity, chronic pancreatitis, chronic cholecystitis, hypertension, coronary heart disease, etc.), as a result of which patients with GERD should be comprehensive and individualized.

The above data stimulate the improvement of existing and the search for new non-drug technologies for the treatment of GERD, aimed at improving the treatment of primary and concomitant diseases of the digestive system, reducing the dose and time of medication, thereby reducing the number of possible complications.

The effect of these non-drug technologies when used in the treatment of patients with GERD, should consist primarily in the chemical

neutralization of hydrochloric acid, the adsorption of pepsin and bile acids. In addition, they should be characterized by a cytoprotective effect, which is caused by an increase in the content of prostaglandins in the gastric mucosa, stimulation of bicarbonate secretion, and an increase in the production of glycoproteins in the gastric mucus.

Such a mechanism of action is owned by natural healing and preformed physical factors, in particular, medicinal mineral waters (MW).[30, 31] The mechanism of action of MW in its ingestion is associated primarily with the effect on the gastroduodenal hormonal system, leading to the formation of fast and long-term adaptive reactions mediating the body's functioning reserve as a whole.[32] On the other hand, one of the links in the mechanism of the pathogenetic and sanogenetic action of MW, especially with prolonged use, is the accumulation in the body of ions, trace elements and biologically active substances, the specific action of which manifests itself at the system level.[33, 34] According to modern concepts, an important role in the realization of the action of MW when they are used internally is played by the structural features of natural MV, which are characterized by a high degree of organization as an aquatic superstructure with an appropriate ratio of free and bound water and structural units with an adequate amount of dipole, which ensures efficient operation of the mechanisms of absorption and transport of the body.[35]

MW, when used internally by acting on the secretion of gastrointestinal hormones (gastrin, somatostatin), helps to restore impaired physiological functions as a factor not only local but also general effects on the body, causes the inclusion of neurohumoral mechanisms of homeostasis. The features of adaptive rearrangements of most of these hormones correspond to the increase after the use of MW functional reserves of the enteroinsular axis and serotonin-producing intestinal endocrinocytes, which characterizes the effect of MW on the state of the intestinal stress-limiting system, has a regulating effect on restoring the homeostatic balance of the body. So, in the implementation of the therapeutic effect of MW, the ratio of their specific and nonspecific effects on the body is very important against

the background of the general nonspecific effect of MW (the response of the organism is determined by its functional state), specific features are clearly distinguished due to the difference in the chemical composition of MW.[36-38]

The hydrocarbonate anion (HCO_3) in the composition of MW affects protein and carbohydrate metabolism, has anti-inflammatory action, helps to normalize the bile-forming and bile-excreting functions of the biliary system. MW with a predominantly hydrocarbonate anion produces a clear, acid-neutralizing effect in the stomach, has a mild effect in the duodenum. These anions promote the absorption of macro- and trace elements, increase the intensity of oxidation-reduction processes; enhance urinary excretion of the kidneys and promote excretion of the slags. Hydrocarbons in the composition of the MW determine the effect on the interstitial edema of the pancreas associated with a disturbance of the outflow of pancreatic secretion due to inflammatory changes in the mucous membrane of the duodenum that arise when the physiological balance of the acidic and alkaline digestive secretions with a predominance of acid is disturbed.

The presence of sulfate anions (SO_4) in MW gives them pronounced "hepatoprotective" properties expressed in sulfate MW. With their internal coursework, there is a restoration of pigment metabolism, a decrease in signs of a cytolytic syndrome, improvement in bile formation and bile secretion, restoration of hepatic hemodynamics, an increased level of metabolism and intensity of reparative processes.[39, 40] In addition, in terms of its therapeutic effects, MW exceeds many medications. However, they do not have side effects and allergic reactions, overloading the patient's body with chemicals.[41, 42]

Based on the understanding of the etiopathogenetic mechanisms of development and progression of GERD, the basic concept of the research work planned is the introduction of differentiated treatment methods with the phased use of boric bicarbonate, sulphate-bicarbonate mineral waters (total mineralization 5-10 g/L), are directed s to reduce illness episodes, normalization of the acid-forming function of the stomach, the restoration of the functional state hepatopancreatobiliary systems that will enhance the effectiveness

of the treatment, dose reduction acid-suppressive drugs, prevention of progression of inflammatory and erosive changes in the appearance of cancer of the esophagus, as well as improve the quality of life for patients.

Materials and methods

A total of 90 patients with GERD were under observation, 40 women, 50 men.

The study used the following methods: anamnestic, clinical (gastroenterological examination, which assessed the severity of pain, dyspeptic, asthenic syndromes), paraclinical methods (studies of biochemical blood parameters), instrumental (ultrasonographic studies of the digestive system, fibroesophagogastroduodenoscopy with intragastric pH-metric), statistical methods.

The dynamics of the clinical course of GERD with concomitant pathology of the digestive organs was assessed on the basis of a study of the severity of pain, dyspeptic and asthenic syndromes.

The functional state of the liver of patients was assessed on the basis of a study of the most informative biochemical parameters. Liver pigment function was studied by determining unconjugated and conjugated bilirubin using the kinetic method (total bilirubin). Enzyme-forming liver function was investigated by determining the activity of the main enzymes: alanine aminotransferase (ALT) and aspartate aminotransferase (AST). The excretory function was assessed by the level of alkaline phosphatase (APH) and the level of protein metabolism (total protein, albumin). All studies were conducted on the biochemical analyzer "MICROLAB 300".

Gamma-glutamate transferase (GGT), α-amylase level and lipid metabolism (total cholesterol, high-density lipoprotein [HDL], low-density lipoprotein [LDL]) were determined using the enzyme-colorimetric method.

Thymol samples were determined by a photometric method on the spectrophotometer "SF-46."

All patients underwent ultrasonography of the abdominal cavity using the apparatus "HD 3-exp-V2" (Korea).

All patients underwent fibrogastroduodenoscopy (FGDS) on an empty stomach.

The acid-forming function of the stomach was assessed by the method of intragastric pH-metry, which was performed in the morning on an empty stomach. The correct installation of the probe was determined by pH. The level of intragastric pH was determined in basal conditions, after alkaline or stimulation test (bread press).

The average age of patients was (48.2±3.76) years. The concomitant pathology of the digestive organs in the patients was as follows: chronic non-calculous cholecystitis in 70 patients (77.8±4.38)%, chronic pancreatitis in 45 patients (50.0±5.27)%, non-alcoholic fatty liver disease in 65 patients (72. 2±4.72)%. Esophagogastroduodenal pathology in the form of chronic non-atrophic gastritis and duodenitis was diagnosed in 85 patients (94.4±2.41)%. A significant proportion of patients (44.4±5.24)% had complaints characteristic of an asthenic syndrome (general weakness, decreased performance, and rapid fatigue). Mostly these were patients with GERD with concomitant liver steatosis.

Abdominal pain syndrome in the form of pain or severity in the right or left hypochondrium was determined in (77.8±4.38)% of patients.

Manifestations of a dyspeptic syndrome in the form of belching, nausea, abdominal distention, bitter mouth, and burning sensation disturbed all patients. An objective examination of pain in palpation of the right hypochondrium was in (50.0±5.27)% of patients, left hypochondrium in (77.8±4.38)%, an epigastric and pyloroduodenal segment in (94.4±2.41)% of patients. Hepatomegaly, mainly due to the left lobe of the liver, was determined in (72.2±4.72)% of patients.

The study of blood biochemical parameters determined the presence of minimally expressed cholestasis in 65 (72.2±4.72)% of patients, which was characterized by increased levels of APH, GGT, and direct bilirubin. In 10 (11.1±3.31)% of patients, an increase in thymol level was observed, indicating the presence of a mesenchymal-inflammatory reaction in the liver. In 65 (72.2±4.72)% of patients, disorders of lipid metabolism were identified in the form of hypercholesterolemia, hypertriglyceridemia, increased atherogenicity, disorders of LDL and HDL.

During the ultrasound examination of abdomi-

nal organs, it was found that in 65 (72.2±4.72)% of the patients examined, the liver was evenly enlarged in size. Ultrasonographic signs of gall-bladder pathology in the form of thickening of the walls of more than 4 mm were noted in 70 patients (77.8±4.38)%. Signs of chronic pancreatitis in the form of diffuse changes and heterogeneity of the pancreas structure were diagnosed in (50.0±5, 27)% of cases.

The acid-forming function of the stomach on an empty stomach at the start of treatment corresponded to the values of hypoacidism in (44.4±5.24)% of patients, slightly acidic in (33.3±4.97)% of patients, moderately acidic in (22.2±4.38)% of patients. After the stimulation test, pH values corresponded to the value of hypoacidism in (55.5±5.24)% of patients, and absolute hyperacidity in (44.4±5.24)% of patients.

After preliminary research, all patients were randomly divided into three groups of 30 people.

The control group (group 1) was represented by 30 patients (20 men and 10 women) who were prescribed a basic treatment complex-dietary and proton pump inhibitor group drugs in the standard dosage: pantoprazole 40 mg in the morning 30 min before meals for 30 days.

Patients of group 2 (30 people, 15 men, 15 women) in addition to the standard course of treatment received boric highly mineralized bicarbonate sodium water. Water was taken internally in three portions, respectively, 60, 45 and 30 minutes before meals. The amount of water was determined at the rate of 1% of body weight, divided into three doses (on average, from 150 ml to 230 ml per reception). The course of treatment was 21-24 days. The chemical formula of boron highly mineralized hydro carbonate sodium water "Polyana Kvasova" is the following:

$$H_3BO_3 \; 0,195 \; M_{10,22} \; HCO3 \; 90 \; Cl \; 10 \; / \; (NA + K) \; 95 \; Ca \; 4 \; Mg \; 1$$
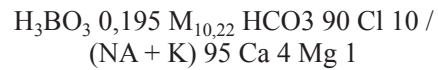
Patients of group 3 (30 people, 15 men, 15 women), in addition to the basic therapy, were prescribed an internal course treatment of highly mineralized sulfate-bicarbonate sodium-magnesium water. The amount of water and the technique of receiving were similar to group 2. The chemical formula of highly mineralized sulfate-hydro carbonate sodium-magnesium water "Donat Mg" is the following:

$$M_{13,28} \; HCO3 \; 90 \; Cl \; 10 \; / \; (NA + K) \; 95 \; Ca \; 4 \; Mg \; 1$$
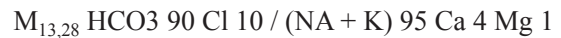
Statistical analysis

The results of clinical and laboratory studies were processed by conventional means of variation statistics, the mean absolute and relative values, their errors, the student's certainty criterion were calculated, the STATEXCEL statistical program was used.

Results

Under the influence of the basic medical complex (group 1), no reliable dynamics of leveling the clinical signs of dyspeptic and asthenic syndromes were determined (Table I). Also unreliable was the dynamics of the severity of objective clinical signs of the disease. At the end of the treatment, with an objective examination, almost

TABLE I.—*The dynamics of the subjective signs of the disease in patients suffering from GERD under the influence of the basic complex of treatment,%, (M±m).*

Complaints	Before treatment	After treatment	P
Pain in the right hypochondrium	53.3±9.11	46.6±9.05	>0.5
Pain in the epigastrium	86.6±6.21	20.0±7.23	< 0.001
Heartburn	100.0±0.00	90.0±5.48	>0.5
Nausea	83.3±6.80	80.0±7.30	>0.5
Belching	83.3±6.80	80.0±7.30	>0.5
Bitter mouth	53.3±9.11	46.6±9.05	>0.5
Flatulence	53.3±9.11	53.3±9.11	>0.5
Diarrhea	50.0±9.13	46.6±9.05	>0.5
Constipation	53.3±9.11	46.6±9.05	>0.5
General weakness	50.0±9.13	36.6±8.80	>0.5

The magnitude of P was calculated between the indicators before and after treatment.

all patients remained sore to palpation of the right and left hypochondrium, pyloroduodenal area, hepatomegaly. The only significant was the reduction of pain abdominal syndrome (Table I).

When conducting a biochemical study of blood serum after one month from the start of treatment in most patients, it was found that impaired liver function remained almost unchanged (Table II). So, in (23.3±7.66)% of patients, an increase in the level of total bilirubin was maintained due to the indirect fraction. In (16.6±6.73)% of patients, signs of the cytolytic syndrome were identified. A third of the patients were diagnosed with cholestasis. Also unreliable was the dynamics of the blood lipid spectrum: total cholesterol (P>0.2), triglycerides (P>0.5), LDL (P>0.2), HDL (P>0.2).

Analysis of the sonographic data did not determine a significant decrease in the pathological size of the liver, a decrease in the level of increased echogenicity in it, an improvement in the passage of the echo signal to the deep layers of the liver, a decrease in volume and sediment in the gallbladder, a decrease in the inflammatory process in the pancreas (P>0.5).

According to FGDS, signs of non-atrophic gastritis and duodenitis were observed in 25 patients (83.3±6.80)%, duodenogastric reflux in 100% of patients.

The pH indicators on an empty stomach at the beginning of treatment in (40.0±8.94)% of patients corresponded to the hypoacid value, in

the remaining patients (60.0±8.94)% the values were slightly acidic and moderately acidic. After the stimulation test (grain extraction), the pH values corresponding to the value of hypoacidity in 50% of patients, and in the other 50%-to the value of absolute hyperacidity. At the end of treatment in 50% of patients, the fasting pH values corresponded to the value of anacidism, in the remaining 50% of patients the value was slightly acidic. After the stimulation test, the pH values corresponded to the hypoacid value in 25 (83.33±6.80)% of patients, in 5 (16.67±6.80)% of patients-with the value of normal-acidity.

Thus, the use of the basic treatment complex for a month in patients with GERD contributed to a significant decrease in the acid-forming function of the stomach, but did not lead to a significant leveling of the signs of dyspeptic (P>0.5) and asthenic (P>0.2) syndromes, signs of cytolytic (P>0.5), mesenchymal-inflammatory (P>0.5), and cholestatic (P>0.5), syndromes, to the positive dynamics of the blood lipid spectrum, restoration of the echo structure of the liver, gallbladder and pancreas.

In patients of group 2, under the influence of the treatment complex, there was a significant decrease in the severity of clinical signs (Table III). This occurred in the form of a decrease in dyspeptic and painful abdominal syndromes. Also significant was the reduction in the severity of objective signs of the clinical course of the disease (Table III). So, at the end of treat-

TABLE II.—*Dynamics of the functional state of the liver in patients suffering from GERD under the influence of the basic complex treatment, (M±m).*

Index	Before treatment	After treatment	P
Thymol test, e.u.	4.28±0.44	4.19±0.22	>0.5
Total bilirubin, μmol /L	17.92±2.07	18.04±2.15	>0.5
AlAT, e./L	38.62±2.31	37.81±2.16	>0.5
AsAT, e./L	37.79±2.11	36.98±2.14	>0.5
APh, e./L	107.44±6.15	102.39±5.98	>0.5
γGT, e./L	48.33±4.09	40.04±3.75	>0.1
α-amylase, e./L	67.29±5.27	65.98±5.16	>0.5
Total protein, g/L	78.24±4.11	77.19±5.43	>0.5
Total cholesterol, mmol/L	6.72±0.14	6.45±0.12	>0.1
ß-lipoproteins, од.	72.15±2.37	69.11±2.24	>0.2
Triglycerides, mmol/L	2.08±0.13	1.98±0.09	>0.5
Low density lipoproteins, mmol/L	4.26±0.19	3.99±0.14	>0.2
High density lipoproteins, mmol/L	1.58±0.06	1.62±0.07	>0.5
Atherogenic coefficient	4.25±0.33	4.16±0.27	>0.5

The magnitude of P was calculated between the indicators before and after treatment.

TABLE III.—*The dynamics of the subjective signs of the disease in patients suffering from GERD under the influence of the course intake of boron highly mineralized sodium bicarbonate water,%, (M±m).*

Complaints	Before treatment	After treatment	P
Pain in the right hypochondrium	46.6±9.05	33.3±8.61	>0.5
Pain in the epigastrium	83.3±6.80	20.0±7.23	<0.001
Heartburn	100.0±0.00	50.0±9.13	<0.001
Nausea	83.3±6.80	50.0±9.13	<0.005
Belching	83.3±6.80	66.6±8.61	>0.2
Bitter mouth	53.3±9.11	46.6±9.05	>0.5
Flatulence	53.3±9.11	53.3±9.11	>0.5
Diarrhea	50.0±9.13	46.6±9.05	>0.5
Constipation	53.3±9.11	46.6±9.05	>0.5
General weakness	50.0±9.13	33.3±8.60	>0.5

The magnitude of P was calculated between the indicators before and after treatment.

TABLE IV.—*Dynamics of the functional state of the liver in patients suffering from GERD under the influence of the course intake of boron highly mineralized sodium bicarbonate water,%, (M±m).*

Index	Before treatment	After treatment	P
Thymol test, e.u.	4.33±0.42	4.10±0.27	>0.5
Total bilirubin, μmol /L	18.95±2.05	18.00±2.10	>0.5
AlAT, e./L	39.62±2.35	36.81±2.15	>0.5
AsAT, e./L	38.72±2.10	36.95±2.12	>0.5
APh, e./L	105.40±6.10	100.35±5.95	>0.5
γGT, e./L	48.35±4.05	40.00±3.72	>0.1
α-amylase, e./L	67.25±5.25	60.90±5.10	>0.1
Total protein, g/L	77.24±4.10	77.18±5.40	>0.5
Total cholesterol, mmol/L	6.70±0.12	6.45±0.10	>0.1
ß-lipoproteins, e.	71.15±2.35	68.11±2.24	>0.2
Triglycerides, mmol/L	2.05±0.15	1.97±0.09	>0.5
Low density lipoproteins, mmol/L	4.23±0.14	3.99±0.14	>0.2
High density lipoproteins, mmol/L	1.57±0.05	1.62±0.07	>0.5
Atherogenic coefficient	4.22±0.33	4.15±0.27	>0.5

The magnitude of P was calculated between the indicators before and after treatment.

ment, with an objective examination, almost all patients showed a decrease in the manifestations of pain during palpation of the epigastrium, left hypochondrium, pyloroduodenal area.

When conducting biochemical studies of blood serum after a month from the start of treatment in the majority of patients in this group, the manifestations of impaired liver function remained almost unchanged (Table IV). Thus, in (40.00±8.95)% of patients, an increase in the level of total bilirubin was maintained due to the indirect fraction. Signs of the cytolytic syndrome were identified in (20.00±7.30)% of patients. One-third of the patients were diagnosed with cholestasis. Also unreliable was the dynamics of the blood lipid spectrum: the concentration of total cholesterol (P>0.1), β-lipoproteins (P>0.2), triglycerides (P>0.5), LDL (P>0.2), HDL (P>0.2).

Analysis of the sonographic data did not determine a significant decrease in the pathological size of the liver, a decrease in the level of increased echogenicity in it, an improvement in the passage of the echo signal to the deep layers of the liver, a decrease in volume and sediment in the gallbladder (P>0.5). Significant was the dynamics to reduce the inflammatory process in the pancreas (P<0.005).

According to FGDS, signs of non-atrophic gastritis and duodenitis were observed in 23 patients (76.7±7.72)%, duodenogastric reflux in 100% of patients.

At the end of the treatment course, the pH indicators on an empty stomach in (50.00±9.13)% of patients corresponded to the hypoacid value, in the remaining patients — (50.00±9.13)% of patients — to the values of absolute normoacid.

After the stimulation test (grain extraction), the pH values corresponding to the hypoacidity value in 2 (6.67±4.55)% of patients, and in other (93.33±4.55)% of patients, with the value of normal-acidity.

Thus, the internal intake of boron highly mineralized sodium bicarbonate water for one month in patients with GERD led to a reliable leveling of signs of abdominal pain (P<0.001) and dyspeptic (P<0.001) syndromes, normalization of the acid-forming function of the stomach. At the same time, reliable dynamics in the elimination of signs of cytolytic (P>0.5), mesenchymal-inflammatory (P>0.5) and cholestatic (P>0.5), syndromes, significant changes in the lipid spectrum of the blood, restoration of liver echostructure, the gallbladder was not observed.

In group 3 after treatment, patients were almost not disturbed by the subjective manifestations of a dyspeptic syndrome (P<0.001), such as heartburn, nausea, sour belching, and bitter taste in the mouth. Periodic short-term pain of low intensity in the area of the epigastrium and right hypochondrium was disturbed only by 6.66%, although the objective manifestations of the pathological process, namely, palpation pain in the epigastric and pyloroduodenal regions remained in 26.66% of people (Table V).

On the part of the biochemical indicators of the functional state of the liver (Table VI), there was a significant decrease in the concentration of total bilirubin (P<0.05) and a tendency to leveling cholestasis in the form of a decrease in the concentration of GGT and alkaline phosphatase (P>0.05).

A significant therapeutic effect was observed on the dynamics of the decrease in the activity of aminotransferases (P<0.005).

Positive changes in the blood lipid spectrum

TABLE V.—*The dynamics of the subjective signs of the disease in patients suffering from GERD under the influence of the course intake of highly mineralized sulphate-bicarbonate sodium-magnesium mineral water,%, (M±m).*

Complaints	Before treatment	After treatment	P
Pain in the right hypochondrium	43.3±9.05	16.6±6.80	<0.005
Pain in the epigastrium	60.0±8.94	0±0	<0.001
Heartburn	63.3±8.79	6.6±4.55	<0.001
Nausea	30.0±8.37	6.6±4.55	<0.05
Belching	30.0±8.37	0±0	<0.05
Bitter mouth	33.3±8.61	10.0±5.47	<0.05
Flatulence	23.3±7.72	16.6±6.80	>0.05
Diarrhea	10.0±5.47	2. 6±4.55	>0.05
Constipation	33.3±8.61	0±0	<0.001

The magnitude of P was calculated between the indicators before and after treatment.

TABLE VI.—*Dynamics of the functional state of the liver in patients suffering from GERD under the influence of the course intake of highly mineralized sulphate-bicarbonate sodium-magnesium mineral water,%, (M±m).*

Index	Before treatment	After treatment	P
Total bilirubin, μmol /L	24.33±2.45	16.87±2.16	<0.05
APh, e./L	148.34±5.23	129.62±5.49	>0.05
γGT, e./L	59.23±5.63	42.48±5.20	>0.05
AlAT, e./L	1.12±0.08	0.72±0.09	<0.05
AsAT, e./L	0.78±0.05	0.48±0.06	<0.005
α-amylase, e./L	129.49±5.26	80.59±4.43	<0.02
Total protein, g/L	71.78±4.40	74.9±4.27	<0.5
Total cholesterol, mmol/L	6.24±0.31	5.28±0.26	<0.05
ß-lipoproteins, *e.*	64.06±3.85	57.37±2.42	>0.05
Triglycerides, mmol/L	2.23±0.11	2.02±0.09	>0.05
Low density lipoproteins, mmol/L	4.22±0.29	3.15±0.24	<0.02
High density lipoproteins, mmol/L	1.43±0.22	1.51±0.19	<0.1
Atherogenic coefficient	3.32±0.23	2.68±0.21	>0.05

The magnitude of P was calculated between the indicators before and after treatment.

were characterized by a significant decrease in the concentration of total cholesterol (P<0.05) and LDL (P<0.02), a tendency to a decrease in ß-LP, triglycerides, and atherogenicity.

Considering that LDL is a fraction of lipids, which provides a proatherogenic profile, we consider it particularly important to reduce their level by 25.35%.

In parallel, there was an improvement in the ultrasound picture of the hepatobiliary system, namely, a tendency to a decrease in the acoustic density of the liver parenchyma and a decrease in the size of inflammatory foci, an improvement in the echo passage to the deep layers of the liver, restoration of gallbladder size (8.39±0.37) sm3 against (9.44±0.62) sm3 (P>0.05).

At the end of treatment, the pH values on an empty stomach in (83.33±6.80)% of patients corresponded to the value of selective normacidity, in the remaining patients — (16.67±6.80)% — absolute normoacidism.

After the stimulation test (grain extraction), the pH values corresponding to the value of normal acidity in (100.00±0.00)% of patients.

Discussion

Thus, internal exchange treatment of highly mineralized sulfate-hydro carbonate sodium-magnesium water Donat Mg helps to improve the clinical course of the underlying disease (elimination of signs of dyspeptic and pain syndromes), concomitant pathology of the esophagogastroduodenal system: normalization of the functional state of the liver as a possible recovery of the pigment metabolism, as a possible restoration of the pigment metabolism, as a possible restoration of pigment metabolism, normalization of the liver, gastroduodenal system the activity of aminotransferases, a decrease in the concentration of total cholesterol and a pronounced decrease in the level of LDL, trends in recovery of indicators of cholestasis, level of TG, ß-lipoproteins and atherogenicity. No significant effect on HDL is noted.

The obtained data are confirmed by sonography: there is a recovery in the size of the gallbladder, an improvement in the acoustic density of the liver parenchyma and the passage of an echo signal into its deep layers.

Conclusions

At the end of treatment, the use of the basic complex of treatment for a month in patients with GERD did not lead to a significant levelling of signs of dyspeptic (P>0.5) and asthenic (P>0.2) syndromes, signs of cytolytic (P>0.5), mesenchymal-inflammatory (P>0.5), and cholestatic (P>0.5), syndromes, significant dynamics from the lipid blood spectrum, recovery of the echo structure of the liver, gall bladder and pancreas.

The use of boron highly mineralized sodium bicarbonate water during the month in patients with GERD led to a significant levelling of signs of abdominal pain (P<0.001) and dyspeptic (P<0.001) syndromes, improvement of acid-forming function of the stomach, but no reliable dynamics were observed in eliminating signs of cytolytic (P>0.5), mesenchymal inflammatory (P>0.5) and cholestatic (P>0.5), syndromes, as well as significant changes in the lipid spectrum of the blood, restoration of echostructure of the liver and bile wow bubble.

Application of highly mineralized sulfate-hydrocarbonate sodium magnesium water improves the clinical course of the underlying disease (elimination of dyspepsia and pain syndromes), concomitant pathology of the esophagogastroduodenal system, the biliary system, normalization of the functional state of the liver in the form of a possible recovery of the pigmentary metabolism, normalization of the activity of aminotransferases, reduction of the concentration of total cholesterol and a marked decrease in the level of LDL cholesterol, the trend towards recovery of hall performance stasis, TG levels, ß-lipoproteins and atherogenic factor. A significant influence on HDL level has not been noted.

A comparative analysis in groups of patients with GERD with concomitant pathology of the digestive system demonstrated an improvement in the clinical course of the main and concomitant diseases, in particular, reliable (P<0.001) levelling signs of asthenic, pain, and dyspeptic syndromes in all patients. At the same time, it should be noted that only in group 3 of patients was the elimination of signs of intestinal dyspepsia.

It should be noted that in the overwhelming majority of patients in groups 2 and 3, by attract-

ing MW to the course, it was possible to prevent the occurrence of undesirable side effects of drug therapy, namely dyspeptic syndrome.

Improving the clinical signs of the disease was accompanied by the restoration of the functional state of the liver. Positive changes in lipid metabolism occurred in most patients of the above groups. But a more significant decrease in the concentration of TH ($P<0.001$) and probably the dynamics of all lipidogram parameters were determined in patients of group 3. Only in this group of patients was the cytolytic syndrome disappeared.

The dynamics of the sonographic picture of the abdominal cavity was characterized by a decrease in the acoustic density of the liver parenchyma and a decrease in the size of the inflammatory foci, an improvement in the echo signal passing to the deep layers of the liver, and an improvement in the visualization of the organ vessels in most of the patients examined, indicating an improvement in the state of the pancreatobiliary system.

At the end of treatment in patients with groups 2 and 3, the pH values on an empty stomach corresponded to the values of selective normalcy and moderate hypoacidity.

Thus, the obtained data confirm the prospects of using highly mineralized mineral waters in the complex treatment of GERD patients.

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