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Clinical and Pathogenetic Aspects of the Course of Peptic Ulcer Disease with Concomitant Duodenal Stasis

Abstract

The aim of the study was to evaluate the features of the course of peptic ulcer disease with concomitant duodenal stasis according to clinical, electrophysiological and morphological studies. **Materials and methods.** The study enrolled 169 patients with duodenal ulcer disease, from whom two groups were formed: the observation group consisted of 107 patients with duodenal ulcer disease with concomitant duodenal stasis; the comparison group included 62 patients with duodenal ulcer disease without concomitant duodenal stasis. The control group consisted of 30 healthy individuals who did not have gastrointestinal complaints. The results of physical examination, laboratory and diagnostic tests were used to verify peptic ulcer disease and duodenal stasis. To study the closing function of the pylorus, the ratio of intraduodenal to intragastric pressure was used. The «Gastroskan-5M» device was used to assess gastric acid production, and the GEM-01 «Gastroskan-GEM» device (Istok-Sistema, Fryazino) was used to study the motor function of the stomach. The mucus-producing function was evaluated using the «Sialo-Test» (Scientific and Production Center (SPC) Eco-Service, St. Petersburg). **Results.** Patients with peptic ulcer disease with concomitant duodenal stasis had more long-term ulcer history — 10.2 ± 1.2 years, compared to patients with ulcer disease without concomitant duodenal stasis — 9.6 ± 1.3 years ($p = 0.041$). Complications were found in 33 (30.8%) patients with peptic ulcer disease with concomitant duodenal stasis, and in 4 (6.4%) patients with peptic ulcer disease without concomitant duodenal stasis ($\chi^2 = 20.9$, $p = 0.017$). Patients of the observation group were more likely to have erosive-ulcerative lesions of the mucosa than patients in the comparison group were (86 (81.2%) and 23 (37.8%) patients, respectively ($\chi^2 = 33.4$, $p < 0.001$)). The ratio of intraduodenal to intragastric pressure in patients of the observation group was significantly lower compared to the control group ($p = 0.0025$). In case of peptic ulcer disease with duodenal stasis, according to «Gastroscan-GEM» data, the Pi/Ps (Pi — electrical activity of each organ of the gastrointestinal tract, Ps — summary level of electrical activity of gastrointestinal tract) coefficient in the stomach increased postprandially by 3.5 times compared with the control group. The total level of sialic acids was significantly higher in patients of the observation group than in the control group ($p < 0.001$) and the comparison group ($p < 0.001$). **Conclusion.** By acting on the main etiopathogenetic aspects of ulcerogenesis, concomitant duodenal stasis exacerbates peptic ulcer disease and increases the frequency of its complications.

Key words: *Peptic ulcer disease, gastric and duodenal motor function, duodenal stasis*

PUD — peptic ulcer disease, DS — duodenal stasis, FGDS — fiberoptic gastroduodenoscopy

The incidence of peptic ulcer disease (PUD) is still high and is one of the leading causes of temporary incapacity for work and disability among people suffering from gastrointestinal disorders. Despite the downward trend in the incidence of peptic ulcer disease, noted by Russian and foreign authors, there has been no decrease in the incidence of complications [1, 2]. This is probably due to a lack of adequate attention to factors contributing to PUD when examining patients, as well as

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the fact that not all pathogenetic mechanisms are taken into account when implementing therapeutic and preventive measures.

The functional state of the duodenum is of great importance in the pathogenesis of the pathology of the gastric and choledochopancreatic zones [3]. In addition to the vital endocrine function, the duodenum coordinates the functions of external and internal secretion of the pancreas and biliary system and regulates the secretory and motor functions of the stomach [4]. At present, the motor function of the gastroduodenal zone is not studied when examining patients with PUD in everyday clinical practice due to the limitation of the methodological approaches. At the early stages, functional disorders of the duodenum are difficult to diagnose due to the absence of pathognomonic clinical symptoms.

The aim of the study was to investigate the features of the course of peptic ulcer disease in combination with duodenal stasis based on clinical, electrophysiological and morphological investigations.

Materials and Methods

One hundred and sixty-nine patients with duodenal ulcer disease (DUD) were monitored. All patients were divided into 2 groups: the observation group consisted of 107 patients with DUD with concomitant duodenal stasis (DS), the comparison group included 62 patients with DUD without concomitant DS. The control group (c) consisted of 30 healthy individuals (mean age 40.5 ± 13.47 years, 10 (33.3%) women, 20 (66.7%) men).

In the observation group (1), the mean age of the patients was 37.1 ± 13.8 years (52 (48.2%) women, 55 (51.8%) men), and in the comparison group (2) — 40.3 ± 14.5 years (24 (38.4%) women and 38 (61.6%) men). All patients in the three groups were comparable by age (ρ_{1-2} = 0.104, ρ_{1-c} = 0.198, ρ_{2-c} = 0.889) and by gender (χ^2= 3.34, ρ_{1-2} = 0,067, χ^2= 2.59, ρ_{1-c} = 0.114, χ^2 = 0.16, ρ_{2-c} = 0.687).

The results of clinical, laboratory and diagnostic tests were used for the verification of DUD with DS. The main diagnostic endoscopic criteria for DS were the presence of bile in the stomach in the fasted state, constant duodenogastric reflux (DGR), dilated and bile-filled duodenum, pyloric incompetence, yellow-green color of the mucous lake, yellow staining of gastric mucus with thickening of the stomach walls, petechiae, erythema and increased volume of gastric contents [5]. Diagnoses were made in accordance with the recommendations of the Russian Gastroenterological Association of the Ministry of Health of the Russian Federation [6].

The "Gastroskan-5M" (Istok-Sistema, Fryazino) device was used to study the secretory function of the stomach and duodenum. This device enables to assess the basal level of acidity in the antrum, cardia and body of the stomach [7].

The level of sialic acids in the submucous layer of the stomach was determined using the "Sialo-Test" (SPC Eco-Service, St. Petersburg) to assess the mucus-producing function [8]. The following were used to diagnose Helicobacter pylori (HP) infection: histological examination (Romanovsky staining), urease test ("HELPIL test", Association of Medicine and Analytics, St. Petersburg), enzyme-linked immunoassay (ELISA, "HelicoBest — antibodies", ZAO VECTOR-BEST, Novosibirsk) and polymerase chain reaction (PCR, "HELICOPOL", Lytech, Moscow) [9].

The Waldman apparatus (venous tonometer) was used to determine the intragastric and intraduodenal pressure [10]. The closing function of the pylorus was evaluated using the ratio of intraduodenal to intragastric pressure [11].

The motor function of the stomach and duodenum was evaluated using the GEM-01 "Gastroscan-HEM" device (Istok-Sistema, Fryazino). The obtained electrogastroenterograms determined the type of electrical activity curve: normokinetic, hyperkinetic, or hypokinetic. The following parameters were evaluated: Pi, Pi/Ps(%), Pi/P(i+1), and rhythm factor, where Pi is the electrical activity of each organ of the gastrointestinal tract (GIT), Pi/Ps is the percentage contribution of each frequency spectrum to the total spectrum, Pi/P(i+1) is the ratio of the electrical activity of the overlying organ to the underlying organ, Kritm is the rhythm factor, which is the ratio of the length of the spectral envelope of the examined section to the width of its spectral section. All parameters were investigated in the fasted state and postprandially. Normally, there is a postprandial increase in the electrical activity of the stomach by 1.5 times, lasting at least 5–7 minutes from minutes 10–14 to minutes 16–22 of the study. The duodenum responds to food stimulation from minutes 14–16 [12].

Statistical processing of the obtained data was carried out using Excel®2016, IBM SPSS v. 17.0. The sample size was determined with the statistical significance level of the study ρ = 0.80, using IBM SPSS. The normality of the distribution of characteristics was determined by the Kolmogorov—Smirnov test. If the distribution differs from normal, the data are presented as median (Me) and interquartile range (IQR). In a normal distribution, the data are presented as arithmetic mean (M), standard deviation (σ). The statistical significance of differences (ρ) was evaluated using the Mann—Whitney test (U) for quantitative characteristics; for qualitative characteristics — nonparametric Pearson's Chi-squared (χ^2) test; with the number of expected observations of up to 5, Yates correction for Chi-squared was used. Differences were considered reliable at significance level ρ < 0.05.

The patients were examined after signing a Patient Informed Consent per the order No. 3909n of the Ministry of Health and Social Development of the Russian Federation of April 23, 2012, (approved by the Ministry of Justice of the Russian Federation on May 5, 2012 under No. 240821), in compliance with ethical principles.

Results

Patients with DUD and concomitant DS had a longer ulcerative history (10.2 ± 1.2 years) than patients with DUD without concomitant DS (9.6 ± 1.3 years) (ρ = 0.041). In 104 (97.2%) patients of the observation group, exacerbations of the ulcer were not seasonal, but 61 (98.3%) patients in the comparison group reported spring-autumn exacerbations (χ^2 = 27.9, ρ = 0.008). More patients with DUD and DS had substance abuse (smoking, alcohol abuse) and a hereditary burden compared with patients with DUD without DS (Table 1).

When compiling the social portrait, it was found that the majority of patients in the observation group — 81 (73.9%) — were office workers with a sedentary lifestyle, and only 26 (26.1%) patients were manual workers. In the comparison group, 44 (70.7%) patients were manual workers (χ^2 = 28.5, ρ = 0.0021). DUD complications (bleeding, perforation) over a ten-year period were revealed in 33 (30.8%) patients with DUD and concomitant DS, and in 4 (6.4%) patients with DUD without concomitant DS (χ^2 = 20.9, ρ = 0.017).

The pain was constant in 40 (37.2%) patients of the observation group in contrast to 8 (12.9%) patients in the comparison group (χ^2 = 5.15, ρ = 0.023). Most often the pain was localized in the epigastric region — in 48 (44.9%) patients (χ^2 = 20.63, ρ < 0.001) (Tab. 2).

In the observation group, 61 (57%) patients reported bitter belching, and in the comparison group — 1 (2%), χ^2= 51.8, ρ = 0.001 (Tab. 3). Bitter taste in the mouth was reported by 83 (77.6%) patients in the observation group versus 8 (12.9%) patients in the comparison group (χ^2= 66.53, ρ < 0.001). Heartburn was observed in 86 (80.4%) patients with DUD with concomitant DS, which was significantly more frequent than in patients with DUD without DS (23; 37.0%), χ^2= 20.2, ρ < 0.001.

Asthenic syndrome, which manifests as fatigue, irritability, apathy, and insomnia, was observed in 44 (40.8%) patients in the observation group. Asthenic syndrome was observed less often in the comparison group — in 17 (27.1%) patients; χ^2= 34.2, ρ < 0.001.

According to fiberoptic gastroduodenoscopy (FGDS) results, the ulcers in 95 (88.7%) patients in

Table 1. *General characteristics of patients*

Parameter	Patients with DUD and DS (observation group) (n = 107) n (%)	Patients with DUD without DS (comparison group) (n = 62) n (%)	χ^2	ρ
Spring-autumn exacerbation	3 (2.8%)	61 (98.3%)	27.9	0.008
Smoking	85 (79.6%)	37 (60.6%)	16.8	0.034
Alcohol	61 (57.3%)	8 (12.2%),	18.3	<0.001
Hereditary burden	74 (69.4%)	12 (19.2%).	20.1	<0.001

Note to Table 1: DUD — duodenal ulcer disease, DS — duodenal stasis, χ^2 — Pearson's Chi-squared test, ρ — reliability, n — number of patients

Table 2. *Pain syndrome in patients with DUD*

Parameter	Characteristic	Patients with DUD and DS (observation group) (n = 107) n (%)	Patients with DUD without DS (comparison group) (n = 62) n (%)	χ^2	p
Localization	epigastric region	48 (44.9)	50 (80.6)	20.63	<0.001
	paraumbilical	15 (14.0)	7 (11.3)	0.258	0.611
	right/left hypochondrium	31 (29.0)	10 (16.1)	3.52	0.060
Time of occurrence	in the fasted state	18 (16.0)	35 (65.5)	28.63	<0.001
	postprandial	49 (45.7)	19 (30.6)	2.52	0.112
	permanent	40 (37.2)	8 (12.9)	5.15	0.023
Acuity	acute	39 (37.2)	23 (37.1)	0.206	0.650
Intensity	intense	38 (35.1)	24 (38.7)	0.173	0.678
Painless ulcer		13 (12.1)	0 (0)	2.37	0.139

Note to Table 2: DUD — duodenal ulcer disease, DS — duodenal stasis, χ^2 — Pearson's Chi-squared test, p — reliability, n — number of patients

Table 3. *Dyspepsia in patients with DUD*

Parameter	Characteristic	Patients with DUD and DS (observation group) (n = 107) n (%)	Patients with DUD without DS (comparison group) (n = 62) n (%)	χ^2	p
Belching	air	12 (11.2)	20 (32.3)	11.32	0.001
	eaten food	1 (0.9)	20 (32.3)	35.39	<0.001
	bitterness	61 (57.0)	1 (1.6)	51.86	<0.001
Heartburn		86 (80.4)	23 (37.1)	32.107	<0.001
Bitterness in the mouth		83 (77.6)	8 (12.9)	66.53	<0.001

Note to Table 3: DUD — duodenal ulcer disease, DS — duodenal stasis, χ^2 — Pearson's Chi-squared test, p — significance, n– number of patients

the observation group were localized in the duodenal bulb, without significant difference with the comparison group. The average size of the ulcerous lesion in the observation group was smaller than in the comparison group (0.56 ± 0.23 and 0.81 ± 0.31 cm, respectively, p = 0.001). In 73 (68.2%) patients with DUD with DS, "kissing" ulcers were observed in the duodenal bulb. In 15 (24.2%) patients of the comparison group, the ulcers were round, in 30 (47.6%) — "crateriform", and in 17 (28.2%) — had an irregular shape. Erosive-ulcerative lesions of the mucosa were more often in the observation group than in the comparison group (86 (81.2%) and 23 (37.8%) patients, respectively, $\chi^2 = 33.4$, $p < 0.001$) (Fig. 1). In DUD with concomitant DS, the ulcers had a small diameter, but a deep base compared with the comparison group, which usually had larger isolated, ulcers.

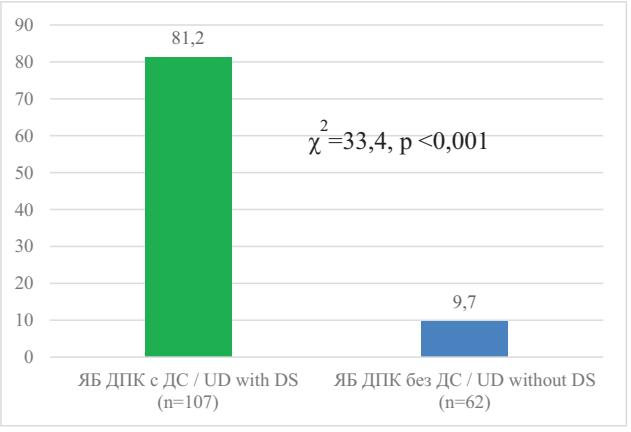

Figure 1. *The combination of ulcer with erosions. p – significance of difference between groups according to Pearson's Chi-squared test (χ^2) ($p < 0.05$)*

DUD — duodenal ulcer disease, DS — duodenal stasis.

According to the histological analysis, in patients with DUD and DS, atrophy was detected in 45 (42.0%) patients, gastric metaplasia — in 6 (5.6%) patients. In the comparison group, atrophy was observed in 12 (19.3%) patients ($\chi^2 = 35.5$, $p < 0.001$), and metaplasia was not detected.

Abdominal manometry showed a significant increase in intragastric pressure in the observation group — up to 119 (IQR: 114–126) mm of water and intraduodenal pressure to 168 (IQR: 165–172) mm of water, respectively, compared with the control group (70 (IQR: 57–74.8) and 116 (IQR: 111.9–124), $p = 0.001$). The ratio of intraduodenal to intragastric pressure, which is indicative of the closing function of the pylorus, was significantly lower in the DUD with DS group compared with the control group: 1.26 (IQR: 1.19–1.32) and 1.7 (IQR: 1.0–2.4), respectively, $p = 0.0025$. There were no changes in the group of patients with DUD without DS in comparison with the control group ($p = 0.9$).

In the observation group, the Pi/Ps coefficient in the stomach postprandially increased by 3.5 times (Table 4). The rhythm coefficient of the duodenum after food stimulation decreased significantly — by 2.9 times compared with the control group (0.3 ± 0.01 and 0.87 ± 0.05, respectively, $p < 0.001$), which indicates a hypokinetic type of curve of duodenal electric activity. In the comparison group,

Table 4. *Gastric and duodenal electrical activity in patients with DUD and DS*

Parameter	Gastroduodenal region	In the fasting state		p	Postprandially		p
		Patients with DUD and DS (observation group) (n = 107) (M ± σ)	Control group (n = 30) (M ± σ)		Patients with DUD and DS (observation group) (n = 107) (M ± σ)	Control group (n = 30) (M ± σ)	
Pi/Ps (%)	Stomach	13.6 ± 0.58	23.6 ± 9.5	< 0.001	46.5 ± 5.8	24.1 ± 1.8	<0.001
	Duodenum	4.4 ± 1.02	2.1 ± 0.68	< 0.001	1.7 ± 0.07	2.18 ± 0.17	<0.001
Pi/P (i+1)	The stomach/duodenum ratio	6.7 ± 0.38	10.4 ± 5.7	< 0.001	17.43 ± 2.46	10.2 ± 4.2	<0.001
Kritm	Stomach	4.7 ± 2.42	4.85 ± 2.1	0.883	3.9 ± 0.11	4.71 ± 0.18	0.001
	Duodenum	0.72 ± 0.12	0.9 ± 0.5	0.013	0.3 ± 0.01	0.87 ± 0.05	<0.001

Note to Table 4: the parameters obey normal distribution (according to the Kolmogorov—Smirnov test); they are presented as M — arithmetic mean, σ — standard deviation), p — significance of differences between the corresponding and control groups of patients (according to Student's t-test)
DUD — duodenal ulcer disease, DS — duodenal stasis, n — number of patients

Table 5. *Gastric and duodenal electrical activity in patients with DUD without DS*

Parameters	Gastroduodenal region	In the fasting state		p	Postprandially		p
		Patients with DUD without DS (comparison group) (n = 62) (M ± σ)	Control group (n = 30) (M ± σ)		Patients with DUD without DS (comparison group) (n = 62) (M ± σ)	Control group (n = 30) (M ± σ)	
Pi/Ps (%)	Stomach	43.6 ± 7.8	23.6 ± 9.5	<0.001	48.05 ± 4.9	24.1 ± 1.8	<0.001
	Duodenum	2.23 ± 0.4	2.1 ± 0.68	0.087	14.32 ± 2.3	2.18 ± 0.17	<0.001
Pi/P (i+1)	The stomach/duodenum ratio	39.6 ± 0.48	10.4 ± 5.7	<0.001	11.2 ± 0.9	10.2 ± 4.2	0.051
Kritm	Stomach	5.7 ± 1.03	4.85 ± 2.1	0.53	5.17 ± 2.11	4.71 ± 2.11	0.171
	Duodenum	0.86 ± 0.11	0.9 ± 0.5	0.723	0.94 ± 0.28	0.87 ± 0.05	0.252

Note to Table 5: the parameters obey normal distribution (according to the Kolmogorov—Smirnov test); they are presented as M — arithmetic mean, σ — standard deviation, p — significance of differences between the corresponding and control groups of patients (according to Student's t-test)
DUD — duodenum ulcer disease, DS — duodenal stasis, n — number of patients

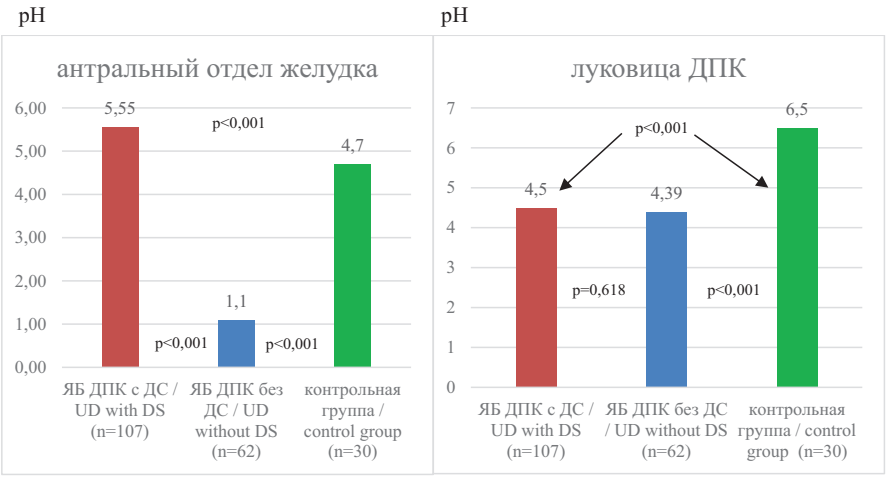

Figure 2. *pH levels in the antrum and duodenal bulb. ρ – significance of differences between groups according to Student's t-test (ρ < 0.05)*

DUD — duodenal ulcer disease, DS — duodenal stasis, n — number of patients

the coordination of the stomach and duodenum operation was preserved (Pi/P(i+1) — 11.2 ± 0.9) and postprandially corresponded to the normokinetic type (Table. 5).

During endoscopic pH-metry, intragastric pH was significantly higher in the DUD with DS group than in healthy individuals (5.55 ± 1.31 and 4.7 ± 0.4, respectively, $p < 0.001$), and pH in the duodenum was lower than in the control group (4.5 ± 0.99 and 6.5 ± 0.28, respectively, $p < 0.001$), which is apparently associated with the violation of the closing function of the pylorus (Fig. 2). Compared to the control group, the comparison group showed a significant decrease in gastric pH (4.7 ± 0.4 and 1.1 ± 0.23, respectively, $p < 0.001$), which was caused by an increase in the acid-producing function of the stomach and acidification of the duodenum (6.5 ± 0.28 and 4.39 ± 0.43, respectively, $p < 0.001$).

There were fewer patients infected with HP in the observation group than in the comparison group: 77 (71.9%) and 57 (91.9%) patients, respectively, $\chi^2 = 10.0$, $p < 0.001$. The observation group had a significantly higher level of sialic acids than the comparison group (4.1 (IQR: 3.9–4.3) and 3.1 (IQR: 2.9–3.3) mmol/l, respectively, $p < 0.001$) and the control group (4.1 (IQR: 3.9–4.3) and 2.3 (IQR: 1.6–2.7) mmol/l, respectively, $p < 0.001$).

Discussion

In DUD with concomitant DS, the most typical clinical symptoms and signs of DUD are observed. However, some features of the clinical course of the disease have been identified. Comorbid patients noted the predominance of dyspeptic symptoms over a less intense epigastric pain syndrome compared to the comparison group. DS can be asymptomatic for a long time [13, 14], but in combination with DUD, changes in the motor function of the stomach and duodenum largely manifest as dyspepsia. Gastroparesis, which is observed in a varying degree with DS, manifests as "stomach pains".

The prevalence of asthenic syndrome, which manifests as apathy, increased irritability and rapid fatigue in patients with DUD, is explained by chronic intoxication with stagnation of the duodenum content and duodenal hormone insufficiency [15].

Studies in patients with DUD and concomitant DS showed significant impairment of the motor function of the stomach and duodenum. An increase in the Pi/P(i+1) ratio in patients with DUD and concomitant DS indicates the discoordination of the motor function of the gastroduodenal zone due to a decrease in the ratio of electrical activity between the stomach and the duodenum, which does not create the necessary pressure gradient [16]. The multidirectional activity of the stomach and duodenum is also indicated by a change in the rhythm factors.

The prolonged stasis of the infected contents in the duodenum is a predictor of chronic atrophic duodenitis [17]. In patients with DS, duodenogastric reflux causes damage to the gastric mucosa by bile acids and lysolecithin, which, according to our data, leads to the development of intestinal metaplasia [18].

The progression of DUD is the final point of the vicious circle of excessive acidification of the duodenum due to a decrease in the closing function of the pylorus (hypersecretory, biliary, pancreatic, enteric, or mixed).

DS in case of DUD has an adverse effect on the protective properties of the mucous barrier of the gastroduodenal zone [19], which was confirmed in our study by an increase in the content of total sialic acids in mucus, which are indicators of the proteolysis process.

The etiological role of HP decreases in case of DUD in combination with DS. Our work showed the new pathogenetic factors of DS that contribute to the formation of duodenal ulcers, accompanied by frequent exacerbations and complications.

Conclusions

1. Duodenal stasis significantly exacerbates peptic ulcer disease by affecting the main etiopathogenetic aspects of ulcerogenesis.
2. Peptic ulcer disease concomitant with duodenal stasis is characterized by erosive and ulcerative lesions of the stomach and the duodenum, which is the equivalent of a deep pathological process in the gastroduodenal zone.
3. Concomitant duodenal stasis is an important factor that increases the incidence of peptic ulcer disease complications.

Author Contribution:

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication.

Vakhrushev Ya.M. — contribution to the development of the concept and design, interpretation and critical analysis of the results, articulation of conclusions, editing, final approval for publication.

Busygina M.S. (ORCID ID: https://orcid.org/0000-0003-1740-2391): collecting and processing the materials, writing.

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