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GENESIS OF GASTROINTESTINAL TRACT LESIONS IN RHEUMATOLOGICAL PATIENTS.

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Annotation

The pathogenesis of damage to the gastrointestinal tract in rheumatological patients at the onset of the disease, according to modern literature, has not been sufficiently studied, and the conclusions are also not clear. This article presents the results of studies of the state of the gastrointestinal tract in rheumatological patients at the onset of the disease and during treatment with basic drugs and NSAIDs. The study revealed clinical and functional changes in the gastrointestinal tract, an imbalance between protective factors and aggressive factors, and determined their role in the development of the pathological process in the digestive tube.

Keywords

Gastroduodenal Pathology, gastric juice, insoluble mucous gel of the stomach lining, rheumatological diseases, non-steroidal anti-inflammatory drugs.

Introduction. As follows from the analysis of modern literature, rheumatic diseases (RD) are in one of the first places in terms of the level of their negative impact on modern society, despite the successes achieved both in the diagnosis and treatment of these diseases, the number of patients is not decreasing [1, 2, 3], on the contrary, the incidence of complications from various organs and systems is increasing (EULAR-2020.). There remains a high trend in the prevalence of RD in the world, and the incidence rate among the population of various countries reaches up to 30 - 40%

[1, 3, 5, 6].

Analysis of the structure of the incidence of RD, according to the official statistics of the republic, although indicates a relative decrease in the growth rate of morbidity among the population, there are many problems, the solution of which requires in-depth scientific research, both in the direction of timely diagnosis of

visceral manifestations, and in the development of new approaches to treatment of RD, taking into account possible complications.

One of the most common complications in RD that influence the effectiveness of treatment is the occurrence and progression of secondary changes in the gastrointestinal tract [4,7, 8]. Gastrointestinal lesions in rheumatic diseases are determined by the close relationships between the etiological and pathogenetic mechanisms of gastroenterological and rheumatic diseases [7], which can explain both the possibility of the existence of gastrointestinal lesions within the framework of the main rheumatic disease (for example, gastrointestinal lesions in systemic scleroderma), and the existence of rheumatic disease as an extraintestinal manifestation gastroenterological pathology (erythema nodosum in Crohn's disease). In some cases, it is difficult to determine which pathological process is primary.

It is necessary to take into account the possibility of secondary lesions of the gastrointestinal tract as a complication caused by the action of the drugs used for treatment, among which NSAIDs have priority [4, 8, 9].

According to the literature, when taking NSAIDs, "NSAID gastropathy" occurs in 60 to 70% of cases, and the largest share among these lesions is occupied by erosive and ulcerative processes, the frequency of which is 50% and 25%, respectively. The medical and social significance of the problem is so great that rheumatologists call NSAID gastropathy the "second rheumatic disease" [10,11,16].

The risk of developing side gastroduodenal effects increases significantly with the simultaneous administration of basic therapy drugs, primarily corticosteroids and anticoagulants [12].

The relevance of this problem is due to the extremely widespread use of NSAIDs; about 30 million people use NSAIDs every day around the world. According to WHO, more than 44 - 50 thousand tons of aspirin alone are consumed in the world, and 24 - 30 thousand tons of paracetamol. In the USA alone, more than 19 billion are sold per year. NSAID tablets. However, even short-term administration of small standard doses of NSAIDs can cause damage to the gastrointestinal mucosa, impaired renal function and other complications, which often pose a serious threat to the health and life of patients [4, 13].

It has now been established that while taking NSAIDs, lesions of any part of the gastrointestinal tract can develop - from the lower third of the esophagus (in the presence of gastroesophageal reflux) to the distal parts of the colon [14, 15]. The issue of secondary changes in the gastrointestinal tract also needs to be addressed; is this the result of a side effect of NSAIDs or is there a possibility of initial damage to various parts of the gastrointestinal tract in conditions of RD.

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The study of the morphofunctional state (MFS) of the gastrointestinal mucosa in relationship is necessary for a comprehensive assessment of the general condition of patients before treatment. Since, despite the centuries-long history of studying RD with a not fully understood etiology, rather complex pathogenesis and problems of early diagnosis of the disease remain in the focus of attention of the medical community, while aspects of the intersystem relationship are practically not affected. In this study, we tried to study the state of the gastrointestinal tract in patients with RD, as a single and integral system that changes its functional activity and morphostructural characteristics both under the influence of the pathological process and measures aimed at eliminating the pathological process (the effects of basic drugs and NSAIDs), which determined purpose of scientific research.

Purpose of the study: Study of the state of the gastrointestinal tract in rheumatological patients with disclosure of the genesis of damage to the digestive tube based on the identification of clinical, functional, structural, biochemical and endoscopic disorders at the onset of the disease and in patients with a long history of rheumatic fever.

Materials and research methods: The study included patients with rheumatoid arthritis (RA), ankylosing spondylitis (ASA) and osteoarthritis (OA). The paper presents the results of a comprehensive screening examination of 278 patients with RD, of which 84 patients were at the onset of the disease. 194 patients with a long history of the disease from 1 to 5 years, from 5 to 10 years or more. The control group consisted of 40 patients with duodenal ulcer (DU). All three groups of patients were comparable by gender and age.

Today, the diagnosis of RB is carried out according to the criteria of the American Association of Rheumatology (AAR) and the European League of Rheumatology (EULAR).

Endoscopic methods for examining the upper floor of the gastrointestinal tract (esophagus, stomach and duodenum) were carried out using Olympus devices. Gastric juice for bacteriological culture and for analysis of insoluble mucous gels was obtained during EGD through the working channel of the device with a sterile Teflon catheter, and biopsy specimens were simultaneously taken for morphological studies.

For endoscopic examination of the lower floor of the gastrointestinal tract, an Olympus CF-D20 colonofiberscope was used. During the study, biopsies were taken for morphological studies. Endoscopic examinations were documented using a CCTV television system from Olympus.

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The assessment of the motor-evacuation function of the gastrointestinal tract, as well as the anatomical features of the small and large intestines, was carried out on the basis of X-ray studies using barium suspension.

Insoluble mucosal gels (IMGs) were studied in portions of gastric juice. The content of insoluble glycoproteins (IGP) was assessed by the content of its main carbohydrate components - fructose, hexose, hexosamines and sialic acids according to the method of P.D. Rabinovich (1973). The content of sialic acids in a suspension of gastric juice was determined according to the method of L.I. Linevik (1962).

The obtained data were subjected to statistical processing on a Pentium I computer using the Statgraphics software package (USA). The significance of differences (P) was calculated using Student's t-test. Differences were considered significant at $P < 0.05$. The research was carried out in the laboratory of genetics of the Russian Cancer Research Center of the Ministry of Health of the Republic of Uzbekistan.

The obtained research results and their discussion. We studied the possibility of primary gastrointestinal lesions in RB. For this purpose, the examined patients with RD were divided into 2 groups: group 1 - disease debut, group 2 - patients with a long history of RD (recurrently ill and previously treated with NSAIDs and other medications). The first group of patients with the onset of RD - 84 patients, consisted of 67 (79.8%) women aged 18 to 36 years and 17 (20.2%) men aged 20 to 32 years. In this group, 49 (58.3%) patients had a history of gastrointestinal diseases. Of these, 24 (28.5%) had gastritis, 13 (15.5%) had viral hepatitis in childhood, 12 (14.3%) had colitis, and 33 (39%) patients periodically had stool disorders. At the time of the survey, complaints from the gastrointestinal tract were noted in 70% of respondents. At the same time, complaints from the intestines came to the fore: stool disturbances - in 37 (44%), flatulence, transfusion and rumbling in the abdomen were detected in 21 (25%) patients, of the patients with complaints from the gastrointestinal tract, in 26 (30 .9%) there were spastic or periodic cramping pains reported after defecation. 21 (25%) patients complained of heartburn, which was accompanied by a feeling of heaviness in the epigastric region and periodic constipation (Table 1).

Table 1

Frequency of occurrence of certain types of endoscopically (EGDS) gastropathy established by NSAIDs in the RD

Types of gastropathy	Onset		With a long history	
	Number of cases	%	Number of cases	%

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Gastroduodenitis	-	-	19	9,8
Gastritis + GUD+DUD	-	-	21	10,8
Gastritis	13	15,4	39	20,1
Erosion + stomach gastroduodenitis	9	10,7	29	14,9
Erosive esophagitis with gastroduodenitis + GDRD	9	10,7	20	10,3
АГПОД+РЭ	-	-	9	4,6
Duodenal ulcer	5	6	10	5,2
Gastric ulcer	-	-		-
Including the combination of pathology of the GDD	18	21,4	78	40
GDRD	35	42	86	44,3
Without pathology	48	57,2	47	24,3
Total	84	100%	194	100%

Endoscopic studies revealed the presence of endoscopically positive pathology in 36 (42.8%) patients. At the same time, 13 (15.4%) patients had gastritis, 9 (10.7%) patients had a picture of reflux esophagitis in combination with gastroduodenitis, as well as GDRD, 9 (10.7%) had erosive gastritis in combination with GDRD. The presence of an ulcerative scar in the duodenal bulb was determined in 5 (6%) patients at the time of examination. At the time of examination, the endoscopic picture of the esophagus, stomach and duodenum was calm and without any significant changes in 48 (57.2%) patients. However, 26 (55%) of 48 examined patients, without endoscopically detected changes in the gastroduodenal zone, had complaints from the gastrointestinal tract. Consequently, in RB at the onset of the disease, before taking NSAIDs, subjective manifestations of gastrointestinal lesions prevail over objective signs.

The second group was dominated by women 125 (64.4%) aged from 20 to 46 years, men 69 (35.6%) aged from 28 to 53 years.

At the time of the survey, complaints from the gastrointestinal tract were noted by 62% of respondents. The most common complaints were symptoms of gastroesophageal reflux - heartburn (31%), a feeling of heaviness in the epigastric

region (34%), rumbling and bloating (41%). The presence of constipation was detected in 33% of patients, diarrhea - in 14%. Consequently, 47% of the subjects in group 1 had a bowel disorder.

Endoscopic studies showed the presence of gastritis in 39 (20.1%) patients, gastroduodenitis - in 19 (9.8%), erosive gastroduodenitis with combined reflux esophagitis - in 29 (14.9%), the presence of erosive esophagitis with gastroduodenitis, combined with GDRD, was observed in 20 (10.3%) subjects with a long history of rheumatic fever. Axial hiatal hernia and reflux esophagitis were found in 9 (4.6%), acute gastric ulcers and duodenal ulcers in combination with erosive esophagitis - in 21 (10.8%) patients. At the same time, half of the patients with endoscopically diagnosed duodenal ulcer with erosive esophagitis complained only of heaviness in the epigastric region after eating, despite the presence of pain in the projection of the duodenum upon palpation. Consequently, despite the presence of "obvious" damage to the gastroduodenal zone, patients have virtually no subjective sensations, which may be due to the analgesic and anti-inflammatory effects of NSAIDs.

Indeed, in 78 (40%) patients receiving a combination of indomethacin and hormones, according to endoscopy, the presence of combined pathology of the gastrointestinal tract was noted: pathology of the esophagus, stomach and duodenum. It was established the presence of reflux esophagitis, chronic gastritis with acute, complete and incomplete chronic erosions, mainly in the antrum of the stomach, on the part of the duodenum, the presence of erosive bulbitis, duodenitis and duodenogastric bile reflux (GDRD). In total, 86 (44.3%) patients in this group were found to have BHR. In 10 (5.2%) patients, ulcerative scars were found in the duodenal bulb. Only in 47 (24.3%) patients out of 194 examined in the second group, the endoscopic picture was calm, without any special changes at the time of the examination. However, despite the absence of endoscopic signs of damage to the gastrointestinal tract, 20 patients had complaints from the gastrointestinal tract.

From the presented data, it becomes obvious that in the conditions of the debut of RD, certain shifts take place in the functional activity of the gastrointestinal tract, not only from the proximal, but also from its distal parts. At the same time, the symptom complex from the digestive tract is not identical to the symptom complex that occurs with duodenal ulcer. A distinctive feature of the manifestations of gastrointestinal damage at the onset of RD is the presence of frequent signs of involvement of the large intestine in the pathological process. As the duration of the course of RD lengthens, symptoms from the gastrointestinal tract become more pronounced; a distinctive feature of the symptom complex from the gastrointestinal tract in patients with a long history of RD is a certain

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"smoothing" of manifestations from the distal parts of the digestive tube. Apparently, in the mechanisms of increased gastrointestinal symptoms in this category of patients, a priority role is played by drugs used in the treatment of RD, primarily NSAIDs.

We analyzed the results of X-ray studies of the gastrointestinal tract. At the same time, in patients with the onset of RD, radiological signs of one or another intestinal pathology were found in 75% of cases, in patients with a long history of RD - in 65%. At the same time, among patients in the control group (patients with duodenal ulcer), such signs were found in only 45% of patients. Consequently, in rheumatological patients, both at the onset of the disease and with a long history, radiological signs of damage to the small and large intestines are more common than in duodenal ulcers. In the structure of these pathologies, regardless of the underlying disease, the largest share is occupied by enterocolitis and spastic colitis, and enteritis accounts for the smallest share.

An X-ray examination of the gastrointestinal tract in the examined groups of patients, along with intestinal pathology, revealed signs of impaired motor-evacuation function of the intestine in 35% of patients with the onset of RD, in 40% with a long history of the disease, and in 60% of patients with duodenal ulcer.

As the results of our studies show, RD has clear clinical and functional signs of pathology from the gastrointestinal tract, both at the onset and during the long course of RD.

At the same time, any pathological process, no matter what degree of functional disturbances is accompanied, begins at the level of the biochemical systems of the cell, and after reaching a certain level of disorganization, structural disturbances begin to appear. Based on the above, we studied the state of the protective barrier function of the gastroduodenal zone under conditions of use of NSAIDs that differ in the selectivity of their effect on cyclooxygenase (COX) isoforms.

The studied indicators of the protective barrier function of GDZ, in particular insoluble mucous gel (IMG), depending on the duration of RD, are shown in Figures 1 and 2.

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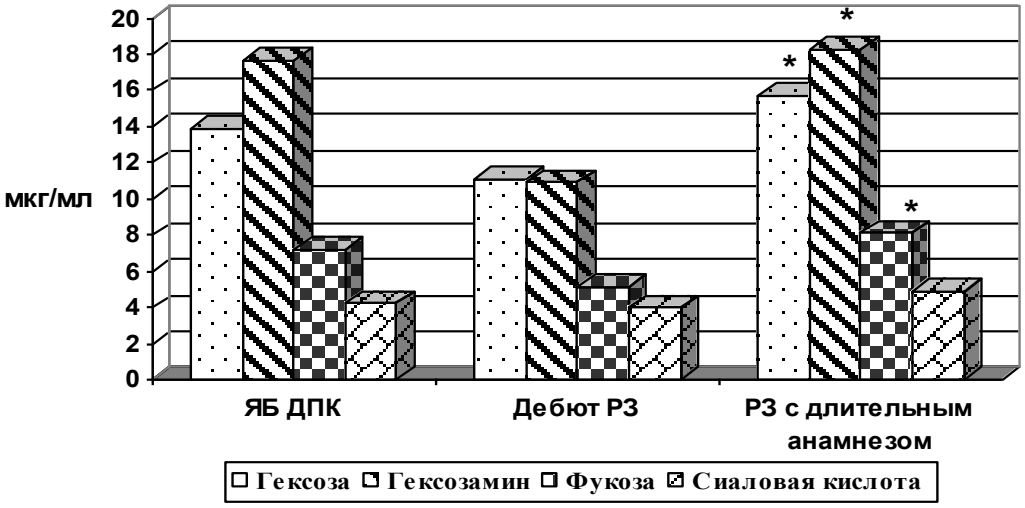
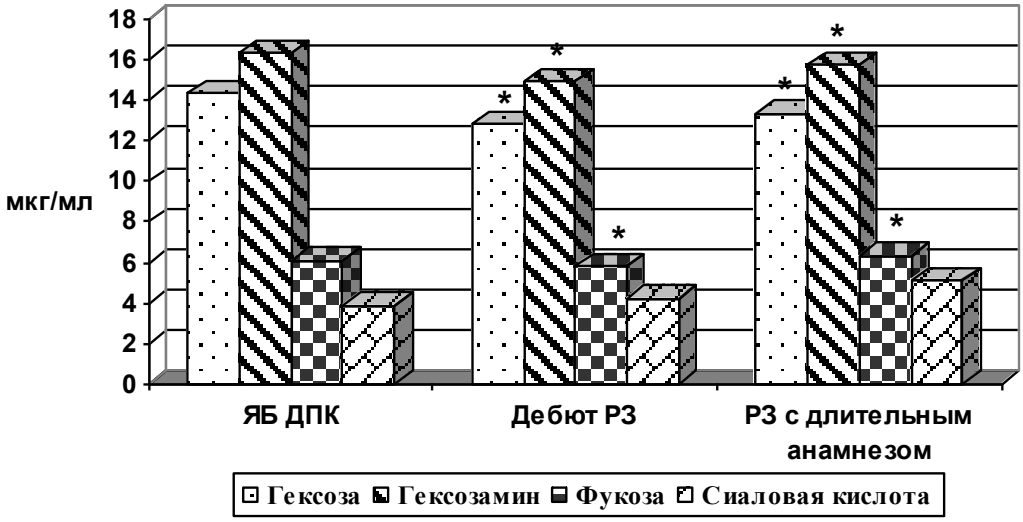


Note: *-P <0.05 significance compared to the onset of RD

Fig 1. Indicators of glycosaminoglycans in portions of gastric juice in rheumatological patients before treatment



Note: *P <0.05 significance compared to the onset of RD

Fig 2. Indicators of glycosaminoglycans in portions of gastric juice in rheumatological patients during treatment

As can be seen from the results obtained in rheumatological patients at the onset of the disease, the content of hexose hexosamine and fructose in portions of gastric juice is comparatively lower than those in patients with peptic ulcer. And the content of sialic acid is comparable to the indicators of patients with peptic ulcer.

In rheumatological patients with a long history of rheumatism while taking medications, the content of the studied glycosaminoglycans in portions of gastric

juice begins to increase. At the same time, as can be seen in Fig. 1, the content of hexose, hexosamine, fructose and sialic acid becomes higher, the indicators in rheumatological patients at the onset of diseases by 41.4%, 67.9%, 58.8% and 22.5%, respectively. Consequently, as the history of rheumatological diseases lengthens, the release of insoluble mucous gel components, in particular glycosaminoglycans, into the gastric juice increases. Moreover, in rheumatological patients with a long history of rheumatism, the severity of this process exceeds the indicators characteristic of patients with peptic ulcer (Fig. 1).

From our results, it becomes obvious that in conditions of rheumatological pathology, there is an increase in the release of NSG components into the gastric juice. This may be due to the functional inferiority of the protective barrier layer of the GDZ, or their increased secretion. Consequently, due to the high loss of NSG components, the epithelial layer of the gastrointestinal tract is "exposed" and the epithelial cells of the mucosa become easily accessible to aggressive influences. As can be seen from the data presented in Fig. 2, against the background of complex treatment, both at the onset of the disease and in rheumatological patients with a long rheumatic history, the content of the studied glycosaminoglycans in portions of gastric juice does not differ significantly from those in patients with duodenal ulcer. Thus, the complex treatment of rheumatological diseases that we use has a corrective effect on the factors of local protection of the gastroduodenal zone. Perhaps the basis for the positive effect of treatment is a decrease in the effect of "aggressive" factors, including basic and symptomatic therapy of rheumatological diseases, on the mucous membrane of the gastroduodenal zone, due to an increase in the protective "potential" of this zone.

As is known, the main reason for the failure of the protective barrier function of the gastrointestinal tract is the aggressive effect of gastric juice components. This circumstance dictates the need to conduct research to study the state of gastric secretory activity in the Republic of Belarus.

It has been established that there is not only an anatomical connection between the organs of the gastroduodenal zone, but also a close functional interaction. Consequently, when disorders arise and develop in one organ of these systems, other, functionally related organs of this zone are also involved in the pathological process. However, these issues of this interaction in the context of the development of RD remain completely unresolved. It is known that bile plays a certain role in the secretory function of the stomach and in the mechanisms of food digestion [16,17]. It has been established that bile components are involved in the activation of pepsinogen and influence the processes of bicarbonate formation [18]. Consequently, bile, converting pepsinogen into active pepsin, ensures the

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proteolytic activity of gastric juice, participates in the metabolism of hydrochloric acid, and becomes a kind of pH regulator of the stomach [19].

We studied the functional state of the stomach, in particular its secretory activity in patients with RD. The results of these studies are presented in Table 2 (before treatment).

Table 2.

Indicators of gastric juice in RD.

Indicators	Before treatment		
	On an empty stomach	Before stimulation (one hour)	After stimulation (per hour)
Amount of gastric juice (ml/hour)	17,93 ±2,41	14,4±1,25	16,6±2,58
Total acidity (mmol/l)	5,71± 0,71	13,48±4,11	12,59±3,21
Free hydrochloric acid (mmol/l)	3,57± 0,29	5,26±2,9	4,82±0,78
Bound hydrochloric acid (mmol/l)	5,71± 0,71	6,52±0,79	6,07±0,55
Acid residue (mmol/h)	0,71± 0,48	1,52±0,54	1,61±0,36

Note: * - significance of difference P <0.05

As can be seen from the presented data, the patients we examined upon admission to the clinic showed noticeable changes in both quantitative and qualitative parameters of gastric juice. At the same time, in servings on an empty stomach the amount of gastric juice is about 18 ml. An hour before stimulation it decreases to 14 ml, and does not change significantly after stimulation. Consequently, the patients we examined have a hyposecretory state. Against the background of reduced secretory activity of the stomach, there are some changes in its acidity. At the same time, in servings on an empty stomach, the total acidity is 5.7 titration units. Before stimulation and after stimulation, this indicator increases. In contrast to total acidity, the values of free hydrochloric acid remain practically unchanged in all portions of gastric juice (Table 2).

The first impression is that with low or normal secretory function of the stomach, it is not possible to implement the mechanism of aggressive action.

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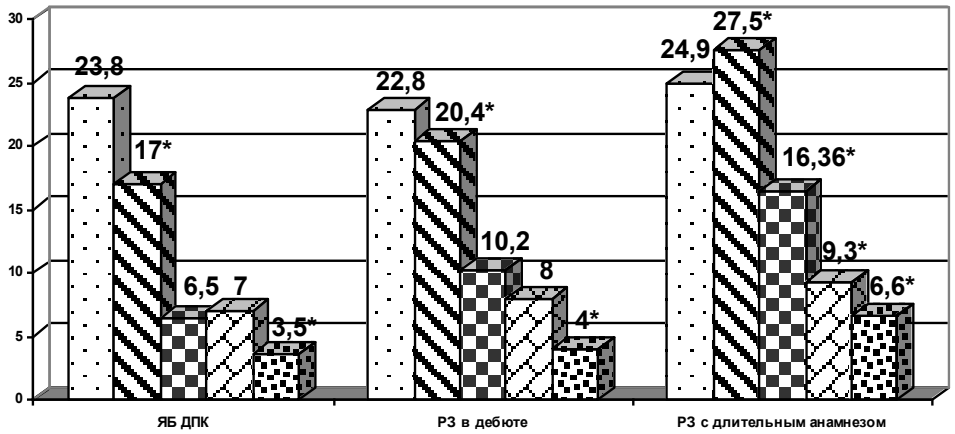
Apparently RB has other reasons or factors, as shown above. The patients examined by us have hypomotor biliary dyskinesia (HBD) and reflux of duodenal contents into the stomach. If we take into account the fact that bile components, in particular bile acids, can participate in the conversion of pepsinogen into pepsin, then it becomes clear the need for BPH, and, consequently, hypomotor dyskinesia. However, bile acids are cellular detergents and can damage the epithelial mucosa, which apparently occurs in the patients we examined in the gastrointestinal tract.



Note: *- P <0.05 significance compared to control

Indicators of gastric juice in RB depending on the duration of the disease
Fig 3.

Conclusion. The results of our research allow us to expand the range of our knowledge on the genesis of the occurrence of lesions from the gastrointestinal tract in the Republic of Belarus, which consists in the fact that initial changes in the digestive tract are caused by systemic damage to its connective tissue stroma, and subsequently damage to its mucous membrane is added by drug aggression. Traditional therapy for RD, while exerting a corrective effect on the immune-inflammatory process, on the one hand, provokes damage to the integumentary epithelium of the gastrointestinal tract, on the other. This circumstance indicates the need for timely diagnosis of gastrointestinal lesions in patients with RD and dictates the advisability of including in complex therapy drugs that have a cytoprotective effect on the gastrointestinal mucosa.

Results:

1. Damage to the digestive tract in patients with rheumatological diseases manifests itself in 32% of cases as pain, in 28% of cases as dyspeptic syndrome and in 40% of cases as irritable bowel syndrome.

2. In conditions of rheumatological diseases, in proportion to the duration of the disease, the secretory activity of the stomach with low acidic activity of gastric juice is suppressed, as well as the protective barrier function of the gastroduodenal zone is suppressed.

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Распространенность ревматических заболеваний в России

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