https://doi.org/10.22416/1382-4376-2025-35-4-7-17
UDC 616.3-085

Potential of Pharmacological Correction of Gastrointestinal Motility Disorders

Vladimir T. Ivashkin[1], Igor V. Maev[2], Alexander S. Trukhmanov[1], Tatiana L. Lapina[1]*, Anastasia I. Dolgushina[3], Oxana Yu. Zolnikova[1], Marina F. Osipenko[4], Diana E. Rumyantseva[1], Vladimir I. Simanenkov[5], Olga A. Storonova[1], Igor B. Khlynov[6], Vladislav V. Tsukanov[7]

[1] *I.M. Sechenov First Moscow State Medical University (Sechenovskiy University), Moscow, Russian Federation*
[2] *Russian University of Medicine, Moscow, Russian Federation*
[3] *South Ural State Medical University, Chelyabinsk, Russian Federation*
[4] *Novosibirsk State Medical University, Novosibirsk, Russian Federation*
[5] *North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russian Federation*
[6] *Ural State Medical University, Yekaterinburg, Russian Federation*
[7] *Federal Research Center "Krasnoyarsk Science Center of the Siberian Branch of the Russian Academy of Sciences", a Separate Subdivision of the Research Institute of Medical Problems of the North, Krasnoyarsk, Russian Federation*

Aim: to present key data on the role of gastrointestinal motility dysfunction in the pathogenesis of functional and organic diseases and the importance of acotiamide in the correction of these disorders and to introduce a resolution of the expert council of the Russian Gastroenterological Association and the Russian Society of Neurogastroenterology and Motility.

Key points. Gastrointestinal motility dysfunction represents a key pathogenetic factor that determines the development and clinical course of a broad range of diseases. Functional dyspepsia and gastroesophageal reflux disease are highly prevalent conditions, and motility impairments, such as impaired gastric accommodation and delayed gastric emptying, account for their frequent co-occurrence in the same patient. For the pharmacotherapy of these diseases, drug products with a prokinetic effect are of substantial importance. Acotiamide has a proven prokinetic effect, improves gastric accommodation and emptying, and reduces the severity of symptoms of postprandial distress syndrome and overlapping manifestations of gastroesophageal reflux disease. In a multicenter Russian study, a response to acotiamide therapy was noted in 74.1 % of patients with postprandial distress syndrome versus 51.9 % in the placebo group ($p < 0.001$). Dysmotility and its association with gastrointestinal symptoms in *H. pylori*-associated dyspepsia, reflux gastritis, and autoimmune gastritis, as well as therapeutic measures to correct these disorders and alleviate symptoms, require further research.

Conclusion. Further research into motility disorders of the gastrointestinal tract will help to elucidate the pathogenesis of a number of functional and organic gastroenterological diseases. The body of evidence from international and local studies confirms the clinical efficacy and safety of acotiamide. Its inclusion in national clinical guidelines justifies the use of the drug product in patients with functional dyspepsia and gastric motility disorders, including cases in combination with gastroesophageal reflux disease.

Keywords: gastrointestinal motility, functional dyspepsia, postprandial distress syndrome, gastroesophageal reflux disease, acotiamide, reflux gastritis, autoimmune gastritis

Conflict of interest: the authors declare no conflict of interest.

For citation: Ivashkin V.T., Maev I.V., Trukhmanov A.S., Lapina T.L., Dolgushina A.I., Zolnikova O.Yu., Osipenko M.F., Rumyantseva D.E., Simanenkov V.I., Storonova O.A., Khlynov I.B., Tsukanov V.V. Potential of Pharmacological Correction of Gastrointestinal Motility Disorders. Russian Journal of Gastroenterology, Hepatology, Coloproctology. 2025;35(4):7–17. https://doi.org/10.22416/1382-4376-2025-35-4-7-17

Возможности фармакологической коррекции нарушений моторики желудочно-кишечного тракта

В.Т. Ивашкин[1], И.В. Маев[2], А.С. Трухманов[1], Т.Л. Лапина[1]*, А.И. Долгушина3, О.Ю. Зольникова[1], М.Ф. Осипенко[4], Д.Е. Румянцева[1], В.И. Симаненков[5], О.А. Сторонова[1], И.Б. Хлынов[6], В.В. Цуканов[7]

[1] *ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет), Москва, Российская Федерация*
[2] *ФГБОУ ВО «Российский университет медицины» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*
[3] *ФГБОУ ВО «Южно-Уральский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Челябинск, Российская Федерация*
[4] *ФГБОУ ВО «Новосибирский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Новосибирск, Российская Федерация*

[5] *ФГБОУ ВО «Северо-Западный государственный медицинский университет им. И.И. Мечникова», Министерства здравоохранения Российской Федерации, Санкт-Петербург, Российская Федерация*
[6] *ФГБОУ ВО «Уральский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Екатеринбург, Российская Федерация*
[7] *ФБГНУ «Федеральный исследовательский центр "Красноярский научный центр Сибирского отделения Российской академии наук"», обособленное подразделение НИИ медицинских проблем Севера, Красноярск, Российская Федерация*

Цель: рассмотреть ключевые данные о роли нарушений моторной функции желудочно-кишечного тракта в патогенезе функциональных и органических заболеваний и значение акотиамида в коррекции данных нарушений, представить резолюцию совета экспертов Российской гастроэнтерологической ассоциации и Российского общества нейрогастроэнтерологии и моторики.
Основные положения. Нарушения моторики желудочно-кишечного тракта являются ключевым патогенетическим звеном, определяющим развитие и клиническое течение широкого спектра заболеваний. Функциональная диспепсия и гастроэзофагеальная рефлюксная болезнь отличаются высокой распространенностью, а двигательные нарушения, такие как нарушение аккомодации желудка и его отсроченное опорожнение, обуславливают их частое сочетание у одного пациента. Для фармакотерапии этих заболеваний существенное значение имеют препараты с прокинетическим эффектом. Акотиамид обладает доказанным прокинетическим действием, улучшает аккомодацию и опорожнение желудка, снижает выраженность симптомов постпрандиального дистресс-синдрома и сочетанных проявлений гастроэзофагеальной рефлюксной болезни. В многоцентровом российском исследовании ответ на терапию акотиамидом отмечен у 74,1 % пациентов с постпрандиальным дистресс-синдромом против 51,9 % в группе плацебо ($p < 0,001$). Нарушения моторики и их связь с гастроинтестинальными симптомами при *H. pylori*-ассоциированной диспепсии, рефлюкс-гастрите и аутоиммунном гастрите, терапевтические мероприятия по коррекции этих нарушений и ликвидации симптомов требуют дальнейших исследований.
Заключение. Дальнейшие исследования нарушений двигательной функции желудочно-кишечного тракта позволят раскрыть патогенез ряда функциональных и органических гастроэнтерологических заболеваний. Совокупность данных международных и отечественных исследований подтверждает клиническую эффективность и безопасность акотиамида, а его включение в национальные клинические рекомендации обосновывает применение препарата у пациентов с функциональной диспепсией и нарушениями моторики желудка, в том числе при сочетании с гастроэзофагеальной рефлюксной болезнью.
Ключевые слова: гастроинтестинальная моторика, функциональная диспепсия, постпрандиальный дистресс-синдром, гастроэзофагеальная рефлюксная болезнь, акотиамид, рефлюкс-гастрит, аутоиммунный гастрит
Конфликт интересов: авторы заявляют об отсутствии конфликта интересов.

Для цитирования: Ивашкин В.Т., Маев И.В., Трухманов А.С., Лапина Т.Л., Долгушина А.И., Зольникова О.Ю., Осипенко М.Ф., Румянцева Д.Е., Симаненков В.И., Сторонова О.А., Хлынов И.Б., Цуканов В.В. Возможности фармакологической коррекции нарушений моторики желудочно-кишечного тракта. Российский журнал гастроэнтерологии, гепатологии, колопроктологии. 2025;35(4):7–17. https://doi.org/10.22416/1382-4376-2025-35-4-7-17

On May 23, 2025, under the leadership of Acade-mician of the Russian Academy of Sciences, President of the Russian Gastroenterological Association Vladimir T. Ivashkin, Expert Council of the Association and the Russian Society of Neurogastroenterology and Motility "The role of motility dysfunction in the development of gastrointestinal tract diseases" was held.

The main functions of the motility of the digestive tract are to ensure the propulsive movement of food, its mixing with digestive secretions and the delivery of substrates for absorption, to prevent retrograde movement and to evacuate undigested residues [1]. Certain disorders of gastrointestinal motility can act as significant pathogenetic factors contributing to the development of many gastroenterological diseases. The group of diseases with primary disturbances of the motility of the digestive tract includes both organic diseases and functional disorders — disorders of the interaction "brain — gastrointestinal tract". The purpose of the Expert Council meeting was to present key data on the role of gastrointestinal motility disorders in the pathogenesis of functional and organic diseases and to review the significance of acotiamide in the management of these disorders. The experts' main focus was on functional dyspepsia (FD) and gastroesophageal reflux disease (GERD).

Functional dyspepsia and gastrointestinal motility disorders

FD is the most common gastroduodenal functional disorder, with a global prevalence in the general population reaching 7.2 % (7.1–7.4 %) based on online surveys and 4.8 % (4.5–5.1 %) based on home interviews. According to clinical variants of FD, the respondents were distributed as follows: postprandial distress syndrome accounted for 66.6 and 59.5 %, epigastric pain syndrome — 15.3 and 28.1 %, and these syndromes overlap — 18.1 and 12.4 % (based on online surveys and home interviews, respectively) [2].

The pathophysiology of FD is multifaceted and includes complex interactions and mutual

influences of various factors. These include gastrointestinal motility disorders, visceral hypersensitivity, changes in barrier function and the gastrointestinal microbiota, dysregulation of the immune system, and disturbances in "brain — gastrointestinal tract interactions" [1, 3–5]. Motility disorders are considered not only as the most important links in the pathogenesis of FD, but also as targets for the drug action of prokinetics in the treatment of this widespread disorder [6, 7].

Experts from the United European Society of Gastroenterology and the European Society of Neurogastroenterology and Motility in a consensus on FD named impaired gastric accommodation and delayed gastric emptying as proven pathophysiological mechanisms of the disease [8].

The gastric accommodation response is a physiological process involving the relaxation of the gastric fundus after a meal, which allows food to be retained in this area. Accommodation disorder — lack of adequate postprandial relaxation of the proximal stomach with rapid entry of food into the antrum, its stretching and development of symptoms of epigastric fullness and early satiety. This movement disorder is detected in FD in 15–50 % of cases and can be observed not only in postprandial distress syndrome, but also in epigastric pain syndrome and their combination. Delayed gastric emptying is considered as a traditional cause of the development of FD symptoms. Delayed gastric emptying has been demonstrated in approximately 30 % of patients with FD and is simultaneously a characteristic sign of gastroparesis [5, 8]. Gastroparesis is defined precisely as a delay in gastric emptying in the absence of a mechanical obstruction. The diagnosis of gastric emptying disorder can be confirmed by esophagogastroduodenoscopy, ultrasound, scintigraphy and a special breath test [9].

It should be noted that delayed gastric emptying and impaired accommodation are not always associated with the development of symptoms. The correlation between gastric emptying rate and the nature or severity of symptoms in FD has been inconclusive [5, 8, 10]. A study involving over 900 patients with upper gastrointestinal symptoms found that, after one year of follow-up, changes in gastric emptying test results led to a revision of the diagnosis from gastroparesis to FD and vice versa in one-third of the patients. It is important to note that this reclassification of diagnoses did not coincide with significant changes in the nature or severity of symptoms [10]. Thus, there is a significant overlap of symptoms between gastroparesis and FD, and their differential diagnosis is a pressing issue [9].

In terms of the development of FD, one cannot fail to mention hypersensitivity to gastric distension, which experts from the European Society of Neurogastroenterology and Motility listed among the proven pathophysiological mechanisms [8]. Increased sensitivity to gastric distension has been found in 34–65 % of patients with FD. Hypersensitivity manifests itself as the perception of normal gastric activity, such as stomach fullness during eating, as uncomfortable or painful, which causes FD symptoms. Hypersensitivity to gastric distension is associated with a higher incidence of postprandial pain, belching, and weight loss, and increased symptom severity correlates with increased visceral sensitivity. The connection between hypersensitivity and the clinical variant of FD has not been established [5, 8].

Combination of gastroesophageal reflux disease and functional dyspepsia

Gastroesophageal reflux disease (GERD) is a chronic organic disease characterized by a primary disorder of the motor-evacuation function of the upper gastrointestinal tract, dysfunction of the esophagogastric junction, and the presence of pathological gastroesophageal reflux. Thus, in GERD, the delay in gastric motor-evacuation function and impaired gastric emptying lead to distension of the gastric walls and an increase in intragastric pressure, which, in turn, triggers transient lower esophageal sphincter relaxations and increases the number of pathological gastroesophageal reflux episodes [11]. Thus, disturbances in gastric accommodation and emptying serve as the basis for the frequent combination of GERD and FD in one patient. According to the meta-analysis, 41.15 % (95 % confidence interval (95%CI): 29.46–53.93 %) of patients with GERD have symptoms of FD, and 31.32 % (95 % CI: 19.43–46.29 %) of patients with FD have symptoms of GERD [12].

In a study of *H. pylori*-negative patients (n = 3085), factors associated with the combination of FD and nonerosive reflux disease compared with individuals without these pathologies included female gender (odds ratio (OR) — 2.08; 95% CI: 1.24—3.52), body mass index < 18.5 (OR = 2.87; 95% CI: 1.56–5.07), alcohol intake ≥ 20 g/day (OR = 1.85; 95% CI: 1.06–3.15), high anxiety level (high score on the State-Trait Anxiety Inventory scale) (OR = 2.53; 95% CI: 1.62–4.00) [13]. In a study of 3281 patients with FD, the most common disease that was combined with FD was GERD (50.69 %). Less frequently, a combination of FD with irritable bowel syndrome (21.46 %) and functional constipation (6.03 %) was established. Risk factors associated with the combination of FD with GERD and other

functional disorders compared with the presence of FD alone were older age, female gender, low body mass index, history of gastroenteritis, anxiety, depression, and poor sleep quality [14]. In a European study, anxiety and depression were also associated with the combination of FD and non-erosive reflux disease [15].

The original data were obtained by conducting not only esophagogastroduodenoscopy, but also pH-impedancemetry and high-resolution esophageal manometry in patients with a combination of FD, established according to Rome IV criteria, and reflux symptoms. In 28.7 % of cases in this group, GERD was reliably confirmed — erosive esophagitis grade B according to the Los Angeles classification or esophageal acid exposure time ≥ 4.2 % were identified. In patients without objective confirmation of GERD during instrumental examination, in 55.1 % of cases the cause of reflux symptoms was functional heartburn, in 16.2 % — hypersensitivity to reflux [16]. These data allow us to re-evaluate the combination of FD with reflux symptoms and define further research prospects for the development of a personalized, comprehensive model for managing such patients [17].

Symptoms of dyspepsia and gastritis of various etiologies

Dyspepsia, functional dyspepsia and H. pylori

The Kyoto Consensus Report on *Helicobacter pylori* gastritis legitimized the term "*H. pylori*-associated dyspepsia", this variant of dyspepsia is considered as a distinct entity. In *H. pylori*-positive patients with dyspepsia, symptoms may be caused by *Helicobacter pylori* gastritis if successful eradication is accompanied by sustained remission. The diagnosis of FD is established if dyspeptic symptoms persist after etiological treatment of bacterial gastritis [18]. Maastricht Consensus VI states that before establishing a reliable diagnosis of FD, *H. pylori*-associated gastritis must be excluded [19].

According to a systematic review evaluating the efficacy of *H. pylori* eradication therapy in the treatment of functional dyspepsia, which analyzed 29 clinical trials involving 6,781 patients, it was demonstrated that eradication therapy is significantly more effective in achieving resolution (number needed to treat — 14; 95% CI: 11–21) or reduction (number needed to treat — 9; 95% CI: 7–17) of dyspeptic symptoms. Thus, it has been shown that the positive effect of anti-Helicobacter therapy in patients with functional dyspepsia is statistically significant, albeit modest [20].

It should be noted that the causes and mechanisms of the occurrence of dyspepsia symptoms in the presence of *H. pylori* and their disappearance or persistence after eradication of the infectious agent have not been revealed and continue to be the subject of discussion and research. Prognostic factors that differentiate *H. pylori*-associated dyspepsia from FD before eradication therapy and the subsequent six-month observation period have not been established [18]. Traditionally, changes associated with *H. pylori* infection have been considered as causative factors of dyspeptic symptoms, such as restructuring of the secretory function of the stomach and chronic inflammation of the gastroduodenal mucosa, including low-grade inflammation, infiltration of enterochromaffin-like and mast cells [21].

Several studies confirm that *H. pylori* infection slows down gastric emptying. In an experiment on mice, B. Liu et al. attempted to elucidate the mechanism underlying this phenomenon: compared to uninfected mice, *H. pylori*-positive animals exhibited delayed gastric emptying accompanied by a reduction in interstitial cells of Cajal in the gastric muscle layer. The authors suggested that this is a consequence of decreased expression of stem cell factor in gastric tissues due to *H. pylori* infection [22]. There are reports that *H. pylori*-positive patients with dyspepsia have been found to have a single nucleotide polymorphism of the *NapA* gene of the Ser70 type, which promotes the activation of neutrophils in the gastric mucosa. It is suggested that neutrophil infiltration of the muscular layer of the stomach, where the pacemaker interstitial cells of Cajal are located, may be associated with gastric motility disorders in patients with dyspepsia [23].

It is obvious that the recognition of the significant role of microbiota in the pathogenesis of FD [3, 5, 9] and the available data on changes in the microbiota of the stomach and gastrointestinal tract as a whole under the influence of the *H. pylori* infection itself and the eradication of the infection [24] determine the directions of future research. Interesting results were obtained by X. Wang et al., who showed that *H. pylori*-positive individuals, compared with individuals without infection, more often had small intestinal bacterial overgrowth (SIBO) (49.1 % vs. 24.5 %; $p = 0.019$), as well as methanogen overgrowth (24.5 % vs. 8.2 %; $p = 0.027$). The presence of SIBO and especially methanogen overgrowth in *H. pylori*-positive patients was associated with more severe gastrointestinal symptoms assessed by the GSRS questionnaire. Interestingly, eradication of *H. pylori* resulted not only in a reduction in symptoms, but also in the disappearance of SIBO and methanogen overgrowth [25].

In a well-known study, which states that duodenal eosinophilia may be a characteristic

symptom in some adult patients with FD, it was stated that no significant relationship was found between *H. pylori* infection and the number of eosinophils in the duodenum ($p < 0.4$), however, in patients infected with *H. pylori*, a significant increase in the number of eosinophils in the gastric mucosa was observed compared to uninfected patients ($p < 0.001$) [26]. F.J. Barreyro et al. analyzed the association between *H. pylori*-associated dyspepsia, *H. pylori* genotype and duodenal eosinophilia. 72 % of *H. pylori*-positive patients with normal esophagogastroduodenoscopy data had complaints characteristic of epigastric pain syndrome, 18 % — characteristic of postprandial distress syndrome, 10 % — of their combination. Histological assessment of chronic inflammation in the duodenum, weak duodenal eosinophilia and intraepithelial lymphocytes did not reveal any differences. Genetic characteristics of strains depending on *oipA* and *vacA* did not affect the severity of chronic inflammation of the duodenal mucosa, the number of eosinophils and intraepithelial lymphocytes. Duodenal eosinophilia was associated with cagA-positive *H. pylori* strains (OR = 4.2; 95% CI: 1.78–9.93) [27].

It is known that certain strains of probiotics and postbiotics can be added to *H. pylori* eradication therapy to reduce the frequency of adverse events and increase the effectiveness of antihelicobacter therapy [19, 28]. In a multicenter Russian study, the combination of the postbiotic *Limosilactobacillus* (*Lactobacillus*) *reuteri DSM*17648 (Helinorm) and standard two-week triple therapy (+ two weeks of postbiotic monotherapy) in patients with FD increased the effectiveness of *H. pylori* eradication (96.7 % in the postbiotic group compared with 86.0 % in the triple therapy group with placebo ($p = 0.039$)) and reduced the frequency of gastrointestinal adverse events [29]. Eradication therapy was prescribed to *H. pylori*-positive patients who had no significant changes at endoscopy and diseases that would explain the presence of dyspepsia symptoms, which allowed the authors to classify them as FD patients based on appropriate criteria. By the end of the course of eradication therapy, both groups showed a significant decrease compared to the baseline level of FD symptoms and most gastrointestinal symptoms, which were assessed using the "7 × 7" and "Gastrointestinal Symptom Rating Scale" questionnaires. By the end of the 4-week follow-up period, this trend had become even more pronounced. These changes in symptoms did not depend on the presence of a postbiotic in the scheme of *H. pylori* eradication therapy [29]. It is interesting to note that a reduction in the severity of gastrointestinal symptoms, primarily epigastric pain, when *L. reuteri DSM*17648 is prescribed both in monotherapy and when this postbiotic is included in eradication therapy has been proven in a number of studies [30–32]. A decrease in symptoms of dyspepsia (as well as other gastrointestinal symptoms) may be either a consequence of *H. pylori* eradication or the effect of *L. reuteri DSM*17648 monotherapy with the formation of coaggregates with *H. pylori*, or a direct effect of the postbiotic on the gastrointestinal microbiota, and possibly motility.

Dyspepsia and motility disorders in autoimmune gastritis

The causes of gastrointestinal symptoms in autoimmune gastritis (AIG) are not well understood, but they are not uncommon in this disease. In patients with a newly diagnosed AIG, symptoms of dyspepsia are not uncommon — epigastric pain occurred in 35.3 % of cases, postprandial fullness in 7.1 %, and early satiety in 10.1 %. A considerable number of patients experienced nausea (22.2 %), heartburn (24.2 %), and regurgitation (12.1 %) [33]. In 379 patients with AIG, gastrointestinal symptoms were detected in 56.7 % of cases, of which 69.8 % had upper gastrointestinal symptoms, 15.8 % had lower gastrointestinal symptoms, and 14.4 % had concomitant upper and lower gastrointestinal symptoms. Dyspepsia of the postprandial distress syndrome type was the most common occurrence (in 60.2 % of symptomatic patients). Factors associated with dyspepsia in AIG included age < 55 years (OR = 1.6; 95% CI: 1.0–2.5), absence of smoking (OR = 2.2; 95% CI: 1.2–4.0), and absence of anemia (OR = 3.1; 95% CI: 1.5–6.4) [34].

The association of dyspeptic symptoms in AIG with upper gastrointestinal motility features is unknown. However, in AIG, delayed gastric emptying has been demonstrated. The median gastric emptying time T½ was 127.43 min (50–953) in patients with AIG and 81 min (21.0–121.6) in patients with FD ($p < 0.001$), and the median percentage of delay after 2 hours was 63.8 % vs. 20.2 % ($p < 0.001$). The gastric emptying time (T½) was significantly affected by the serum gastrin level (OR = 1.002; 95% CI: 1.001–1.004; $p < 0.001$), chronic inflammation (OR = 3.689; 95% CI: 1.44–9.39; $p < 0.001$) and increased degree of gastric mucosal atrophy (OR = 8.96; 95% CI: 2.98–26.93; $p < 0.001$) [35].

Dyspepsia and motility disorders in reflux gastritis

Reflux gastritis occurs with duodenogastric reflux of the contents of the duodenum with bile acids, lysolecithin, and pancreatic enzymes, which leads to the appearance of clinical symptoms, endoscopic and histological changes characteristic of

chemical (reactive) gastritis (gastropathy) [36]. In the Kyoto Consensus, this form is distinguished as "gastritis due to duodenal reflux" [18].

The development of duodenogastric reflux may occur as a result of motor dysfunction caused by surgical interventions or as a primary motor dysfunction with impaired coordination of the motor function of the stomach, duodenum, and gallbladder [36, 37]. Antroduodenal manometry and pH-metry make it possible to establish duodenogastric reflux [36]. With intragastric pH-metry, duodenogastric reflux is defined as an increase in pH in the stomach above 5.0, not associated with food intake. Duodenogastric reflux is considered pronounced if the duration of all refluxes exceeds 10 % of the gastric pH monitoring time.

Clinical manifestations of reflux gastritis are nonspecific, and differential diagnosis with FD and biliary functional disorders presents certain difficulties. A review of data from patients with a diagnosis of FD (n = 262), previously established according to Rome III criteria, allowed to distinguish three groups: "biliary gastropathy" with a sufficient amount of intragastric bile during esophagogastroduodenoscopy and histologically identified chemical gastropathy; "non-biliary gastropathy" with histologically proven chemical gastropathy, but without intragastric bile during esophagogastroduodenoscopy; "without gastropathy" with normal gastric mucosa during histological examination and no visible bile in the stomach during esophagogastroduodenoscopy. It turned out that in patients with "biliary gastropathy" in 68 % of cases there was a history of cholecystectomy, compared with 35 % in "non-biliary gastropathy" and 22 % in individuals "without gastropathy" [38]. It is unlikely that one can agree with the previously established diagnosis of FD in some many patients, as well as with the terms proposed by the authors to characterize subgroups of patients by the presence of biliary reflux, but such diagnostic and terminological heterogeneity characterizes the complexity of the issue under consideration. A consensus on the diagnosis of reflux gastritis is necessary and should include approaches to differential diagnosis with FD and biliary functional disorders, as well as recommendations for drug therapy aimed at normalizing motility.

Acotiamide and its place in the management of diseases with motility dysfunction

Acotiamide (acotiamide hydrochloride trihydrate) exerts a reversible inhibitory effect on acetylcholinesterase activity and acts as an antagonist of inhibitory muscarinic type 2 receptors, thereby enhancing acetylcholine release from presynaptic terminals. Acotiamide does not exhibit affinity for D_2-dopamine and serotonin receptors, which distinguishes it from metoclopramide and domperidone. No less significant is the stimulating effect of acotiamide on ghrelin activity [39, 40].

The triple mechanism of action of acotiamide, involving interaction with M_2 muscarinic acetylcholine receptors and inhibition of acetylcholinesterase, was demonstrated in experimental studies to result in acceleration of delayed gastric emptying and enhanced postprandial gastroduodenal motility [41, 42].

In placebo-controlled studies in patients with FD, using real-time gastric ultrasound with fluid intake [43] and scintigraphy [44] it was possible to demonstrate that acotiamide improves gastric accommodation and accelerates gastric emptying.

Significant experience has been accumulated in the clinical use of acotiamide in FD. As early as 2014, a meta-analysis was published demonstrating the efficacy of acotiamide compared to placebo: the relative risk (RR) for overall symptom improvement was 1.29 (95% CI: 1.19–1.40; $p < 0.00001$; I^2 = 15 %). Moreover, acotiamide is more effective for postprandial distress syndrome symptoms (RR = 1.29; 95% CI: 1.09–1.53; $p = 0.003$; I^2 = 0 %) compared to epigastric pain syndrome (RR = 0.92; 95% CI: 0.76–1.11; $p = 0.39$; I^2 = 0 %). The frequency of adverse events with acotiamide treatment was not different from placebo [45].

A multicenter study was conducted in the Russian Federation, which included 389 patients with postprandial distress syndrome who received acotiamide (Dispevict) 100 mg 3 times a day or placebo for 4 weeks. Response to therapy was observed in 143 (74.1 %) of 193 patients in the acotiamide group compared with 98 (51.9 %) of 189 patients in the placebo group ($p < 0.001$). In contrast to placebo, acotiamide therapy resulted in complete regression and relief of symptoms such as "an annoying feeling of fullness after eating a normal amount of food, affecting daily activities", "an annoying feeling of early satiety (including the inability to eat a normal amount of food)", and "postprandial bloating in the epigastric region". After a course of acotiamide, an improvement in well-being and quality of life was noted in 172 (88.7 %) of 194 patients compared with 131 (69.3 %) of 189 patients in the placebo group ($p < 0.001$) [46].

The results of international and Russian studies and meta-analysis data became the basis for including acotiamide as a drug product with a prokinetic effect in the clinical guidelines "Gastritis and Duodenitis" of the Russian Gastroenterological Association (2024) as a symptomatic treatment for patients with chronic gastritis and symptoms of dyspepsia (especially such as epigastric fullness

and early satiety), including in combination with FD [28].

The frequent combination of FD and GERD in one patient makes it difficult to choose effective drug therapy. Today, the main drug products for the treatment of both diseases are proton pump inhibitors and prokinetics [11, 28, 47]. The use of prokinetics in the treatment of GERD is due to their ability to restore the physiological state of the esophagus, indirectly through the normalization of gastric motility, improving esophageal clearance and reducing the number of transient relaxations of the lower esophageal sphincter. In the Clinical Guidelines of the Russian Gastroenterological Association, Russian Scientific Medical Society of Internal Medicine, Russian Society for the Prevention of Noncommunicable Diseases, and Scientific Community for Human Microbiome Research "Diagnosis and Treatment of Gastroesophageal Reflux Disease", it was stated that prokinetics have the greatest effect precisely when GERD and FD are both present [11].

Acotiamide has been shown to be effective in the treatment of FD and GERD in a number of studies. In a randomized, placebo-controlled study of patients with FD and heartburn that persisted despite treatment, proton pump inhibitors not only reduced postprandial dyspepsia symptoms but also GERD symptoms assessed by a questionnaire. Instrumental studies have shown that treatment with acotiamide reduces the frequency of transient relaxations of the lower esophageal sphincter, increases its pressure and increases esophageal clearance [48]. Patients with GERD who experienced persistent heartburn and acid regurgitation more than twice a week despite treatment with a standard dose of vonoprazan or a proton pump inhibitor for at least 8 weeks were additionally prescribed acotiamide 300 mg/day or placebo for another 2 weeks, in addition to their previously taken medications. It is important to note that patients with GERD simultaneously complained of epigastric pain and burning, epigastric fullness, and early satiety. The rate of improvement in overall well-being was 28.6 % and 14.3 % in the patients receiving acotiamide and placebo, respectively ($p = 0.145$). In patients with nonerosive reflux disease, the rates of improvement in general well-being and regurgitation were higher in the acotiamide group than in the placebo group (29.6 % vs. 7.1 % ($p = 0.030$) and 37.0 % vs. 10.7 % ($p = 0.021$), respectively). Acotiamide significantly reduced the total number of reflux episodes ($p = 0.001$), as well as the number of acid ($p = 0.020$), proximal ($p = 0.007$), and liquid ($p = 0.013$) reflux episodes as measured by pH-impedance [49].

Against the background of acotiamide intake, the level of ghrelin in blood plasma increases [50]. It is assumed that one of the mechanisms for the development of FD is a disruption in the synthesis of acylated ghrelin [51, 52]. In patients with postprandial distress syndrome and nonerosive reflux disease, a significant decrease in the level of this peptide hormone was observed compared to healthy individuals and patients with epigastric pain syndrome [52].

Resolution of the Expert Council

1. Disorders of the gastrointestinal tract motility are a key link that determines the development and course of functional and organic gastroenterological diseases. Functional dyspepsia and gastroesophageal reflux disease, as the most prevalent and frequently overlapping nosological forms, are pathogenetically driven by impaired gastric accommodation and delayed gastric emptying.

2. Eradication of *H. pylori* infection allows differentiation between functional dyspepsia and *H. pylori*-associated dyspepsia. The mechanisms of the occurrence of dyspepsia symptoms in the presence of *H. pylori* and their disappearance or persistence after eradication of the infectious agent have not been elucidated and should be the subject of further research, including the study of direct or indirect influence of *H. pylori* on the gastrointestinal microbiota and motility.

3. Dyspepsia symptoms, which may be associated with motor disfunction, are often observed in patients with autoimmune gastritis and reflux gastritis. Due to the non-specific nature of these symptoms, the differential diagnosis of autoimmune or biliary gastritis with functional dyspepsia is of significant practical importance.

4. Studies of motor function, including antroduodenal manometry and pH-metry, are of interest in autoimmune gastritis and reflux gastritis and may potentially help to objectively assess the efficacy of prokinetic drugs in these diseases.

5. Acotiamide has a proven prokinetic effect, improves accommodation and gastric emptying and reduces the severity of symptoms of functional dyspepsia, including its combination with gastroesophageal reflux disease. The totality of data from international and Russian studies, as well as the inclusion of the drug product in national clinical guidelines, confirm its clinical significance and justified place in modern practice.

References / Литература

1. *Boeckxstaens G., Camilleri M., Sifrim D., Houghton L.A., Elsenbruch S., Lindberg G., et al.* Fundamentals of neurogastroenterology: Physiology/motility — sensation. *Gastroenterology.* 2016:S0016-5085(16)00221-3. DOI: 10.1053/j.gastro.2016.02.030
2. *Sperber A.D., Bangdiwala S.I., Drossman D.A., Ghoshal U.C., Simren M., Tack J., et al.* Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome Foundation Global Study. *Gastroenterology.* 2021;160(1):99–114.e3. DOI: 10.1053/j.gastro.2020.04.014
3. *Stanghellini V., Chan F.K., Hasler W.L., Malagelada J.R., Suzuki H., Tack J., et al.* Gastroduodenal disorders. *Gastroenterology.* 2016;150(6):1380–92. DOI: 10.1053/j.gastro.2016.02.011
4. *Holtmann G., Moniruzzaman M., Shah A.; Australian Gastrointestinal Research Alliance (AGIRA); NHMRC Centre for Research Excellence in Digestive Health.* Decoding the gut-brain axis: A journey toward targeted interventions for disorders-of-gut-brain interaction. *Dig Dis.* 2025;43(3):257–65. DOI: 10.1159/000543845
5. *Oshima T.* Functional dyspepsia: Current understanding and future perspective. *Digestion.* 2024;105(1):26–33. DOI: 10.1159/000532082
6. *Qi Q., Wang N., Liu H., Li Y.* Prokinetics for the treatment of functional dyspepsia: An updated systematic review and network meta-analysis. *BMC Gastroenterol.* 2023;23(1):370. DOI: 10.1186/s12876-023-03014-9
7. *Goelen N., Jones M., Huang I.H., Carbone F., Janssen P., Tack J.* Do prokinetic agents provide symptom relief through acceleration of gastric emptying? An update and revision of the existing evidence. *United European Gastroenterol J.* 2023;11(2):146–62. DOI: 10.1002/ueg2.12362
8. *Wauters L., Dickman R., Drug V., Mulak A., Serra J., Enck P., et al.; ESNM FD Consensus Group.* United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) consensus on functional dyspepsia. *United European Gastroenterol J.* 2021;9(3):307–31. DOI: 10.1002/ueg2.12061
9. *Sato H., Grover M.* Gastroparesis and functional dyspepsia: Spectrum of gastroduodenal neuromuscular disorders or unique entities? *Gastro Hep Adv.* 2023;2(3):438–48. DOI: 10.1016/j.gastha.2022.10.005
10. *Pasricha P.J., Grover M., Yates K.P., Abell T.L., Bernard C.E., Koch K.L., et al.; National Institute of Diabetes and Digestive and Kidney Diseases/National Institutes of Health Gastroparesis Clinical Research Consortium.* Functional dyspepsia and gastroparesis in tertiary care are interchangeable syndromes with common clinical and pathologic features. *Gastroenterology.* 2021;160(6):2006–17. DOI: 10.1053/j.gastro.2021.01.230
11. *Ивашкин В.Т., Трухманов А.С., Маев И.В., Драпкина О.М., Ливзан М.А., Мартынов А.И. и др.* Диагностика и лечение гастроэзофагеальной рефлюксной болезни (Рекомендации Российской гастроэнтерологической ассоциации, Российского научного медицинского общества терапевтов, Российского общества профилактики неинфекционных заболеваний, Научного сообщества по изучению микробиома человека). *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2024;34(5):111–35. [*Ivashkin V.T., Trukhmanov A.S., Maev I.V., Drapkina O.M., Livzan M.A., Martynov A.I., et al.* Diagnosis and treatment of gastroesophageal reflux disease (Clinical guidelines of the Russian Gastroenterological Association, Russian Scientific Medical Society of Internal Medicine, Russian Society for the Prevention of Noncommunicable Diseases, Scientific Community for Human Microbiome Research). *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2024;34(5):111–35. (In Russ.)]. DOI: 10.22416/1382-4376-2024-34-5-111-135
12. *Geeraerts A., Van Houtte B., Clevers E., Geysen H., Vanuytsel T., Tack J., et al.* Gastroesophageal reflux disease functional dyspepsia overlap: Do birds of a feather flock together? *Am J Gastroenterol.* 2020;115(8):1167–82. DOI: 10.14309/ajg.0000000000000619
13. *Fujita T., Umegaki E., Masuda A., Kobayashi M., Yamazaki Y., Terao S., et al.* Factors associated with overlap between functional dyspepsia and nonerosive reflux disease in endoscopy-based *Helicobacter pylori*-uninfected Japanese health checkup participants: A prospective, multicenter cross-sectional study. *Intern Med.* 2024;63(5):639–47. DOI: 10.2169/internalmedicine.1786-23
14. *Long Y.Q., Xu W.L., Li L.X., He H.Q., Wang J.J., Shan G.D., et al.* Characteristics and risk factors of functional dyspepsia fulfilling the Rome IV criteria overlapping with gastroesophageal reflux disease, irritable bowel syndrome, and functional constipation in South China. *J Neurogastroenterol Motil.* 2024;30(2):184–93. DOI: 10.5056/jnm23084
15. *Caballero-Mateos A.M., López-Hidalgo J.L., Torres-Parejo Ú., Hernández-González J.M., Quintero-Fuentes M.D., Caballero-Plasencia A.M., et al.* Risk factors for functional dyspepsia, erosive and non-erosive gastroesophageal reflux disease: A cross-sectional study. *Gastroenterol Hepatol.* 2023;46(7):542–52. DOI: 10.1016/j.gastrohep.2022.12.005
16. *Chen S., Jia X., Zhuang Q., Hou X., Siah K.T.H., Zhang M., et al.* Overlapping reflux symptoms in functional dyspepsia are mostly unrelated to gastroesophageal reflux. *J Neurogastroenterol Motil.* 2025;31(2):218–26. DOI: 10.5056/jnm24091
17. *Byun S.Y., Jung K.W.* Overlap between gastroesophageal reflux disease and functional dyspepsia: Do we need a new management paradigm? *J Neurogastroenterol Motil.* 2025;31(2):129–30. DOI: 10.5056/jnm25030
18. *Sugano K., Tack J., Kuipers E.J., Graham D.Y., El-Omar E.M., Miura S., et al.* Kyoto global consensus report on *Helicobacter pylori* gastritis. *Gut.* 2015;64(9):1353–67. DOI: 10.1136/gutjnl-2015-309252
19. *Malfertheiner P., Megraud F., Rokkas T., Gisbert J.P., Liou J.M., Schulz C., et al.* Management of *Helicobacter pylori* infection: The Maastricht VI/Florence consensus report. *Gut.* 2022:gutjnl-2022-327745. DOI: 10.1136/gutjnl-2022-327745
20. *Ford A.C., Tsipotis E., Yuan Y., Leontiadis G.I., Moayyedi P.* Efficacy of *Helicobacter pylori* eradication therapy for functional dyspepsia: Updated systematic review and meta-analysis. *Gut.* 2022:gutjnl-2021-326583. DOI: 10.1136/gutjnl-2021-326583
21. *Zullo A., Hassan C., De Francesco V., Repici A., Manta R., Tomao S., et al. Helicobacter pylori* and functional dyspepsia: An unsolved issue? *World J Gastroenterol.* 2014;20(27):8957–63. DOI: 10.3748/wjg.v20.i27.8957
22. *Liu B., Dong J., Wang S., Yu H., Li Z., Sun P., et al. Helicobacter pylori* causes delayed gastric emptying by decreasing interstitial cells of Cajal. *Exp Ther Med.* 2021;22(1):663. DOI: 10.3892/etm.2021.10095
23. *Sugiyama T., Shiotani A.* The cutting edge research of functional gastrointestinal disorders in Japan: Review on JGA Core Symposium 2018-2020. *Digestion.* 2021;102(1):6–11. DOI: 10.1159/000510680
24. *Guo Y., Cao X.S., Guo G.Y., Zhou M.G., Yu B.* Effect of *Helicobacter pylori* eradication on human gastric microbiota: A systematic review and meta-analysis. *Front Cell Infect Microbiol.* 2022;12:899248. DOI: 10.3389/fcimb.2022.899248
25. *Wang X., Zhu D., Li S., Dai Y., Teng G., Wang W.* The influence of *Helicobacter pylori* infection and eradication on small intestinal bacterial overgrowth and abdominal symptoms. *Dig Dis Sci.* 2024;69(4):1293–301. DOI: 10.1007/s10620-024-08279-y
26. *Talley N.J., Walker M.M., Aro P., Ronkainen J., Storskrubb T., Hindley L.A., et al.* Non-ulcer dyspepsia and duodenal eosinophilia: An adult endoscopic population-based case-control study. *Clin Gastroenterol Hepatol.* 2007;5(10):1175–83. DOI: 10.1016/j.cgh.2007.05.015
27. *Barreyro F.J., Sanchez N., Caronia M.V., Elizondo K., Jordá G., Schneider A., et al.* Low-grade duodenal eosino-

philia is associated with cagA in *Helicobacter pylori*-related dyspepsia. *J Gastroenterol Hepatol.* 2023;38(2):274–82. DOI: 10.1111/jgh.16051
28. *Клинические рекомендации «Гастрит и дуоденит».* 2024. [Clinical guidelines "Gastritis and duodenitis". 2024. (In Russ.)]. URL: https://cr.minzdrav.gov.ru/preview-cr/708_2
29. *Ivashkin V., Maev .I, Poluektova E., Sinitsa A., Avalueva E., Mnatsakanyan M., et al.* Efficacy and safety of postbiotic contained inactivated *Lactobacillus reuteri (Limosilactobacillus reuteri)* DSM 17648 as adjuvant therapy in the eradication of *Helicobacter pylori* in adults with functional dyspepsia: A randomized double-blind placebo-controlled trial. *Clin Transl Gastroenterol.* 2024;15(9):e1. DOI: 10.14309/ctg.0000000000000750
30. *Buckley M., Lacey S., Doolan A., Goodbody E., Seamans K.* The effect of *Lactobacillus reuteris* upplementation in *Helicobacter pylori* infection: A placebo-controlled, single-blind study. *BMC Nutr.* 2018;4:48. DOI: 10.1186/s40795-018-0257-4
31. *Yang C., Liang L., Lv P., Liu L., Wang S., Wang Z., Chen Y.* Effects of non-viable *Lactobacillus reuteri* combining with 14-day standard triple therapy on *Helicobacter pylori* eradication: A randomized double-blind placebo-controlled trial. *Helicobacter.* 2021;26(6):e12856. DOI: 10.1111/hel.12856
32. *Parth K, Prudhivi R, Palatheeya S, Abbas SK, Varsha K, Niharika BV, Lyngkhoi B.* Efficacy of *Lactobacillus reuteri* supplementation in eradication of *H. pylori*: A comparison study with triple drug therapy. *J Pharm Res Int.* 2021;33(52B):151–9. DOI: 10.9734/jpri/2021/v33i52B33611
33. *Miceli E., Lenti M.V., Padula D., Luinetti O., Vattiato C., Monti C.M., et al.* Common features of patients with autoimmune atrophic gastritis. *Clin Gastroenterol Hepatol.* 2012;10(7):812–4. DOI: 10.1016/j.cgh.2012.02.018
34. *Carabotti M., Lahner E., Esposito G., Sacchi M.C., Severi C., Annibale B.* Upper gastrointestinal symptoms in autoimmune gastritis: A cross-sectional study. *Medicine (Baltimore).* 2017;96(1):e5784. DOI: 10.1097/MD.0000000000005784
35. *Kalkan Ç., Soykan I., Soydal Ç., Özkan E., Kalkan E.* Assessment of gastric emptying in patients with autoimmune gastritis. *Dig Dis Sci.* 2016;61(6):1597–602. DOI: 10.1007/s10620-015-4021-1
36. *Ивашкин В.Т., Маев И.В., Лапина Т.Л., Кучерявый Ю.А., Абдулхаков С.Р., Алексеева О.П. и др. H. pylori*-ассоциированный, постэрадикационный и негеликобактерный гастриты: алгоритм диагностики и лечения (обзор литературы и резолюция Совета экспертов Российской гастроэнтерологической ассоциации). *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2024;34(3):7–23. [*Ivashkin V.T., Maev I.V., Lapina T.L., Kucheryavyy Yu.A., Abdulkhakov S.R., Alekseeva O.P., et al. H. pylori*-associated gastritis, gastritis after *H. pylori* eradication and *H. pylori*-negative gastritis: Algorithm of diagnosis and treatment (Literature review and resolution of the Expert Panel of the Russian Gastroenterological Association). *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2024;34(3):7–23. (In Russ.)]. DOI: 10.22416/1382-4376-2024-34-3-7-23
37. *Livzan M.A., Mozgovoi S.I., Gaus O.V., Bordin D.S., Kononov A.V.* Diagnostic principles for chronic gastritis associated with duodenogastric reflux. *Diagnostics (Basel).* 2023;13(2):186. DOI: 10.3390/diagnostics13020186
38. *Lake A., Rao S.S.C., Larion S., Spartz H., Kavuri S.* Bile reflux gastropathy and functional dyspepsia. *J Neurogastroenterol Motil.* 2021;27(3):400–7. DOI: 10.5056/jnm20102
39. *Nowlan M.L., Scott L.J.* Acotiamide: First global approval. *Drugs.* 2013;73(12):1377–83. DOI: 10.1007/s40265-013-0100-9
40. *Шептулин А.А., Работягова Ю.С.* Современные возможности применения акотиамида в лечении функциональной диспепсии. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2024;34(1):70–5. [*Sheptulin A.A., Rabotyagova Yu.S.* Modern possibilities of using acotiamide in the treatment of functional dyspepsia. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2024;34(1):70–5. (In Russ.)]. DOI: 10.22416/1382-4376-2024-34-1-70-75
41. *Seto K., Sasaki T., Katsunuma K., Kobayashi N., Tanaka K., Tack J.* Acotiamide hydrochloride (Z-338), a novel prokinetic agent, restores delayed gastric emptying and feeding inhibition induced by restraint stress in rats. *Neurogastroenterol Motil.* 2008;20(9):1051–9. DOI: 10.1111/j.1365-2982.2008.01135.x
42. *Matsunaga Y., Tanaka T., Yoshinaga K., Ueki S., Hori Y., Eta R., et al.* Acotiamide hydrochloride (Z-338), a new selective acetylcholinesterase inhibitor, enhances gastric motility without prolonging QT interval in dogs: Comparison with cisapride, itopride, and mosapride. *J Pharmacol Exp Ther.* 2011;336(3):791–800. DOI: 10.1124/jpet.110.174847
43. *Kusunoki H., Haruma K., Manabe N., Imamura H., Kamada T., Shiotani A., et al.* Therapeutic efficacy of acotiamide in patients with functional dyspepsia based on enhanced postprandial gastric accommodation and emptying: Randomized controlled study evaluation by real-time ultrasonography. *Neurogastroenterol Motil.* 2012;24(6):540–5, e250–1. DOI: 10.1111/j.1365-2982.2012.01897.x
44. *Nakamura K., Tomita T., Oshima T., Asano H., Yamasaki T., Okugawa T., et al.* A double-blind placebo controlled study of acotiamide hydrochloride for efficacy on gastrointestinal motility of patients with functional dyspepsia. *J Gastroenterol.* 2017;52(5):602–10. DOI: 10.1007/s00535-016-1260-7
45. *Xiao G., Xie X., Fan J., Deng J., Tan S., Zhu Y., et al.* Efficacy and safety of acotiamide for the treatment of functional dyspepsia: Systematic review and meta-analysis. *Scientific World Journal.* 2014;2014:541950. DOI: 10.1155/2014/541950
46. *Бакулин И.Г., Хлынов И.Б., Саблин О.А., Пахомова И.Г., Павлова Н.В.* Клиническая эффективность применения акотиамида у пациентов с функциональной диспепсией: результаты многоцентрового исследования. *Медицинский совет.* 2023;(13):108–15. [*Bakulin I.G., Khlynov I.B., Sablin O.A., Pakhomova I.G., Pavlova N.V.* Clinical efficacy of acotiamide in patients with functional dyspepsia: Results of a multicenter study. *Medical Council.* 2023;(13):108–15. (In Russ.)]. DOI: 10.21518/ms2023-253
47. *Трухманов А.С., Румянцева Д.Е.* Функциональная диспепсия и гастроэзофагеальная рефлюксная болезнь: от патогенеза к современным возможностям терапии. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2024;34(5):83–92. [*Trukhmanov A.S., Rumyantseva D.E.* Functional dyspepsia and gastroesophageal reflux disease: From pathogenesis to current treatment strategies. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2024;34(5):83–92. (In Russ.)]. DOI: 10.22416/1382-4376-2024-34-5-83-92
48. *Funaki Y., Ogasawara N., Kawamura Y., Yoshimine T., Tamura Y., Izawa S., et al.* Effects of acotiamide on functional dyspepsia patients with heartburn who failed proton pump inhibitor treatment in Japanese patients: A randomized, double-blind, placebo-controlled crossover study. *Neurogastroenterol Motil.* 2020;32(2):e13749. DOI: 10.1111/nmo.13749
49. *Yamashita H., Okada A., Naora K., Hongoh M., Kinoshita Y.* Adding acotiamide to gastric acid inhibitors is effective for treating refractory symptoms in patients with non-erosive reflux disease. *Dig Dis Sci.* 2019;64(3):823–31. DOI: 10.1007/s10620-018-5377-9+
50. *Yamawaki H., Futagami S., Kawagoe T., Maruki Y., Hashimoto S., Nagoya H., et al.* Improvement of meal-related symptoms and epigastric pain in patients with functional dyspepsia treated with acotiamide was associated with acylated ghrelin levels in Japan. *Neurogastroenterol Motil.* 2016;28(7):1037–47. DOI: 10.1111/nmo.12805

51. *Yagi T., Asakawa A., Ueda H., Miyawaki S., Inui A.* The role of ghrelin in patients with functional dyspepsia and its potential clinical relevance (Review). *Int J Mol Med*. 2013;32(3):523–31. DOI: 10.3892/ijmm.2013.1418

52. *Shindo T., Futagami S., Hiratsuka T., Horie A., Hamamoto T., Ueki N., et al.* Comparison of gastric emptying and plasma ghrelin levels in patients with functional dyspepsia and non-erosive reflux disease. *Digestion*. 2009;79(2):65–72. DOI: 10.1159/000205740

Information about the authors

Vladimir T. Ivashkin — Dr. Sci. (Med.), Professor, Academician of the Russian Academy of Sciences, Head of the Department of Internal Diseases Propedeutics, Gastroenterology and Hepatology, Director of V.Kh. Vasilenko Clinic of Internal Diseases Propedeutics, Gastroenterology and Hepatology, I.M. Sechenov First Moscow State Medical University (Sechenovskiy University).
Contact information: ivashkin_v_t@staff.sechenov.ru;
119435, Moscow, Pogodinskaya str., 1, build. 1.
ORCID: https://orcid.org/0000-0002-6815-6015

Igor V. Maev — Dr. Sci. (Med.), Professor, Academician of the Russian Academy of Sciences, Head of the Department of Internal Disease Propaedeutics and Gastroenterology, Russian University of Medicine.
Contact information: igormaev@rambler.ru;
127473, Moscow, Delegatskaya str., 20, build. 1.
ORCID: https://orcid.org/0000-0001-6114-564X

Alexander S. Trukhmanov — Dr. Sci. (Med.), Professor of the Department of Propaedeutics of Internal Medicine, Gastroenterology and Hepatology of the N.V. Sklifosovsky Institute of Clinical Medicine, I.M. Sechenov First Moscow State Medical University (Sechenovskiy University).
Contact information: alexander.trukhmanov@gmail.com;
119435, Moscow, Pogodinskaya str., 1, build. 1.
ORCID: https://orcid.org/0000-0003-3362-2968

Tatiana L. Lapina* — Cand. Sci. (Med.), Associate Professor of the Department of Internal Disease Propaedeutics, Gastroenterology and Hepatology, I.M. Sechenov First Moscow State Medical University (Sechenovskiy University).
Contact information: lapina_t_l@staff.sechenov.ru;
119435, Moscow, Pogodinskaya str., 1, build. 1.
ORCID: https://orcid.org/0000-0003-4456-8725

Anastasia I. Dolgushina — Dr. Sci. (Med.), Head of the Department of Hospital Therapy, South Ural State Medical University.
Contact information: dolgushinaai@yandex.ru;
454092, Chelyabinsk, Vorovskogo str., 64.
ORCID: https://orcid.org/0000-0003-2569-1699

Oxana Yu. Zolnikova — Dr. Sci. (Med.), Professor at the Department of Internal Disease Propaedeutics, Gastroenterology and Hepatology, I.M. Sechenov First Moscow State Medical University (Sechenovskiy University).
Contact information: zolnikova_o_yu@staff.sechenov.ru;
119435, Moscow, Pogodinskaya str., 1, build. 1.
ORCID: https://orcid.org/0000-0002-6701-789X

Сведения об авторах

Ивашкин Владимир Трофимович — доктор медицинских наук, профессор, академик РАН, заведующий кафедрой пропедевтики внутренних болезней, гастроэнтерологии и гепатологии, директор Клиники пропедевтики внутренних болезней, гастроэнтерологии и гепатологии им. В.Х. Василенко, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: ivashkin_v_t@staff.sechenov.ru;
119435, г. Москва, ул. Погодинская, 1, стр. 1.
ORCID: https://orcid.org/0000-0002-6815-6015

Маев Игорь Вениаминович — доктор медицинских наук, профессор, академик РАН, заведующий кафедрой пропедевтики внутренних болезней и гастроэнтерологии, ФГБОУ ВО «Российский университет медицины» Министерства здравоохранения Российской Федерации.
Контактная информация: igormaev@rambler.ru;
127473, г. Москва, ул. Делегатская, 20, стр. 1.
ORCID: https://orcid.org/0000-0001-6114-564X

Трухманов Александр Сергеевич — доктор медицинских наук, профессор кафедры пропедевтики внутренних болезней, гастроэнтерологии и гепатологии Института клинической медицины им. Н.В. Склифосовского, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: alexander.trukhmanov@gmail.com;
119435, г. Москва, ул. Погодинская, 1, стр. 1.
ORCID: https://orcid.org/0000-0003-3362-2968

Лапина Татьяна Львовна* — кандидат медицинских наук, доцент кафедры пропедевтики внутренних болезней гастроэнтерологии, гепатологии, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: lapina_t_l@staff.sechenov.ru;
119435, г. Москва, ул. Погодинская, 1, стр. 1.
ORCID: https://orcid.org/0000-0003-4456-8725

Долгушина Анастасия Ильинична — доктор медицинских наук, заведующая кафедрой госпитальной терапии, ФГБОУ ВО «Южно-Уральский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: dolgushinaai@yandex.ru;
454092, г. Челябинск, ул. Воровского, 64.
ORCID: https://orcid.org/0000-0003-2569-1699

Зольникова Оксана Юрьевна — доктор медицинских наук, профессор кафедры пропедевтики внутренних болезней, гастроэнтерологии и гепатологии, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: zolnikova_o_yu@staff.sechenov.ru;
119435, г. Москва, ул. Погодинская, 1, стр. 1.
ORCID: https://orcid.org/0000-0002-6701-789X

* Corresponding author / Автор, ответственный за переписку

Marina F. Osipenko — Dr. Sci. (Med.), Professor, Head of the Department of Propaedeutics of Internal Diseases, Novosibirsk State Medical University.
Contact information: ngma@bk.ru;
630091, Novosibirsk, Krasny ave., 52.
ORCID: https://orcid.org/0000-0002-5156-2842

Diana E. Rumyantseva — Cand. Sci. (Med.), Physician at the Department of Gastroenterology, V.Kh. Vasilenko Clinic of Internal Diseases Propaedeutics, Gastroenterology and Hepatology, N.V. Sklifosovsky Institute of Clinical Medicine, I.M. Sechenov First Moscow State Medical University (Sechenovskiy University).
Contact information: diana-ryazanceva@yandex.ru;
119435, Moscow, Pogodinskaya str., 1, build. 1.
ORCID: https://orcid.org/0000-0001-7048-0538

Vladimir I. Simanenkov — Dr. Sci. (Med.), Professor of the Department of Internal Medicine, Nephrology, General and Clinical Pharmacology with a course in Pharmacy, North-Western State Medical University named after I.I. Mechnikov.
Contact information: visimanenkov@mail.ru;
191015, St. Petersburg, Kirochnaya str., 41.
ORCID: https://orcid.org/0000-0002-1956-0070

Olga A. Storonova — Cand. Sci. (Med.), Physician of the Functional Diagnostics Department, V.Kh. Vasilenko Clinic of Propaedeutics of Internal Medicine, Gastroenterology and Hepatology, I.M. Sechenov First Moscow State Medical University (Sechenovskiy University).
Contact information: storonova_o_a@staff.sechenov.ru;
119435, Moscow, Pogodinskaya str., 1, build. 1.
ORCID: https://orcid.org/0000-0002-0960-1166

Igor B. Khlynov — Dr. Sci. (Med.), Associate Professor of the Department of Faculty Therapy and Geriatrics, Ural State Medical University.
Contact information: hlinov.doc@yandex.ru;
620028, Ekaterinburg, Repina str., 3.
ORCID: https://orcid.org/0000-0002-0944-9811

Vladislav V. Tsukanov — Dr. Sci. (Med.), Professor, Head of the Clinical Department of Adult and Infant Digestive Pathology, Federal Research Center "Krasnoyarsk Science Center of the Siberian Branch of the Russian Academy of Sciences", a Separate Subdivision of the Research Institute of Medical Problems of the North.
Contact information: gastro@impn.ru;
660022, Krasnoyarsk, Partizana Zheleznyaka str., 3g.
ORCID: https://orcid.org/0000-0002-9980-2294

Осипенко Марина Федоровна — доктор медицинских наук, профессор, заведующий кафедрой пропедевтики внутренних болезней, ФГБОУ ВО «Новосибирский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: ngma@bk.ru;
630091, г. Новосибирск, Красный просп., 52.
ORCID: https://orcid.org/0000-0002-5156-2842

Румянцева Диана Евгеньевна — кандидат медицинских наук, врач отделения гастроэнтерологии клиники пропедевтики внутренних болезней, гастроэнтерологии и гепатологии им. В.Х. Василенко, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: diana-ryazanceva@yandex.ru;
119435, г. Москва, ул. Погодинская, 1, стр. 1.
ORCID: https://orcid.org/0000-0001-7048-0538

Симаненков Владимир Ильич — доктор медицинских наук, профессор кафедры внутренних болезней, нефрологии, общей и клинической фармакологии с курсом фармации, ФГБОУ ВО «Северо-Западный государственный медицинский университет им. И.И. Мечникова» Министерства здравоохранения Российской Федерации.
Контактная информация: visimanenkov@mail.ru;
191015, г. Санкт-Петербург, ул. Кирочная, 41.
ORCID: https://orcid.org/0000-0002-1956-0070

Сторонова Ольга Андреевна — кандидат медицинских наук, врач отделения функциональной диагностики Клиники пропедевтики внутренних болезней, гастроэнтерологии и гепатологии им. В.Х. Василенко, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: storonova_o_a@staff.sechenov.ru;
119435, г. Москва, ул. Погодинская, 1, стр. 1.
ORCID: https://orcid.org/0000-0002-0960-1166

Хлынов Игорь Борисович — доктор медицинских наук, доцент кафедры факультетской терапии и гериатрии, ФГБОУ ВО «Уральский государственный медицинский университет». Министерства здравоохранения Российской Федерации.
Контактная информация: hlinov.doc@yandex.ru;
620028, г. Екатеринбург, ул. Репина, 3.
ORCID: https://orcid.org/0000-0002-0944-9811

Цуканов Владислав Владимирович — доктор медицинских наук, профессор, заведующий Клиническим отделением патологии пищеварительной системы у взрослых и детей, ФБГНУ «Федеральный исследовательский центр "Красноярский научный центр Сибирского отделения Российской академии наук"», обособленное подразделение НИИ медицинских проблем Севера.
Контактная информация: gastro@impn.ru;
660022, г. Красноярск, ул. Партизана Железняка, 3г.
ORCID: https://orcid.org/0000-0002-9980-2294

Authors' contributions

All the authors contributed with data collection and analysis, writing of the manuscript, approving final version and its publication.

Вклад авторов

Все авторы внесли равный вклад в сбор и анализ данных, написание документа, утверждение финальной версии и дали согласие на публикацию.

Submitted: 10.06.2025 Accepted: 02.08.2025 Published: 29.08.2025
Поступила: 10.06.2025 Принята: 02.08.2025 Опубликована: 29.08.2025