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Experience in the Treatment of Irritable Bowel Syndrome Developed after a New Coronavirus Infection (COVID-19)

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Aim. To study the effectiveness of Kolofort® (affinally purified antibodies to tumor necrosis factor α, to the brain-specific protein S-100 and to histamine) in patients with various variants of irritable bowel syndrome (IBS) that developed after a new coronavirus infection (COVID-19).
Materials and methods. Clinical and laboratory data of 32 patients with IBS who had a history of COVID-19 pneumonia were analyzed. Course therapy with Kolofort® is prescribed according to the standard scheme for 3 months. Before and after treatment, the dynamics of the symptoms of IBS was assessed according to the questionnaire, the dynamics of anxiety was assessed according to the Hamilton scale.
Results. There were a statistically significant decrease in the severity of IBS symptoms (normalization of the consistency of the stool, cessation of flatulence, a decrease in abdominal pain; $p < 0.05$) and a decrease in anxiety after the end of treatment.
Conclusions. Kolofort® may be effective in eliminating the symptoms of post-infectious IBS and anxiety that developed after COVID-19.
Keywords: coronavirus infection, irritable bowel syndrome, diagnosis, treatment, Kolofort®
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Опыт лечения синдрома раздраженной кишки, развившегося после перенесенной новой коронавирусной инфекции (COVID-19)

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Цель: в наблюдательном исследовании изучить эффективность применения препарата Колофорт® у пациентов с различными вариантами синдрома раздраженного кишечника (СРК) после перенесенной новой коронавирусной инфекции COVID-19.
Материалы и методы. Проанализированы клинико-лабораторные данные 32 пациентов с СРК, перенесших в анамнезе коронавирусную пневмонию (КТ-1, КТ-2). Курсовая терапия препаратом Колофорт® назначена по стандартной схеме на 3 месяца. До и после лечения оценивали динамику симптомов СРК по опроснику, тревожности — по шкале Гамильтона.
Результаты. По шкалам опросника «боль в животе, уменьшающаяся после дефекации», «нарушение консистенции и/или частоты стула», а также «вздутие живота (метеоризм)» наблюдались статистически значимое снижение симптомов после терапии ($p < 0,05$). После окончания лечения выявлена достоверная позитивная динамика по снижению симптомов СРК: нормализация консистенции стула, прекращение метеоризма, а также снижение тревожности.
Выводы. Препарат, представленный аффинно очищенными антителами к фактору некроза опухоли α (ФНО-α), к мозгоспецифическому белку S-100 и к гистамину, может быть эффективен для устранения симптомов постинфекционного СРК после перенесенной коронавирусной инфекции. Зафиксировано снижение тревожности по шкале Гамильтона.
Ключевые слова: коронавирусная инфекция, синдром раздраженной кишки, диагностика, лечение, Колофорт®
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Introduction

According to the Roman criteria of functional diseases of the digestive organs of the IV revision, they are considered as "disorders of interaction between the brain and the gastrointestinal tract" [1]. Functional diseases, including widespread irritable bowel syndrome (IBS), are based on discoordination of the central and peripheral nervous system with the formation of visceral hypersensitivity, motor disorders gastrointestinal tract, changes in the epithelial barrier, immunity and composition of the gut microbiota [1, 2].

The relationship of the new coronavirus infection (COVID-19) with the development of IBS is the subject of active research. The COVID-19 pandemic and its information support have a negative impact on psychological status. For example, a study of the state of the psycho-emotional sphere of 1210 residents of 194 cities was conducted using on-line survey during the peak of the pandemic in China. More than half (53.8 %) of respondents noted a significant impact of COVID-19 on their psychological state, 16.5 % showed symptoms of depression, 28.8 % did anxiety disorders [3]. SARS-CoV-2, binding to the intestinal receptors of the angiotensin-converting enzyme, can affect the absorption of tryptophan and other amino acids, which also have an antimicrobial effect. Significant changes in the gut microbiota have been noted in patients with COVID-19 [4–6]. SARS-CoV-2 can cause inflammation of the intestinal mucosa and disruption of its epithelial barrier by altering the gut microbiota [4]. Post-infectious IBS after COVID-19 is currently considered a special problem [7].

Patients with functional gastrointestinal disorders (FGID) due to the COVID-19 pandemic are diagnosed with anxiety, especially in self-isolation and forced restrictions on medical facilities. Anxiety disorders in IBS are observed in 20–50 % of patients. Patients with severe IBS often have various mental disorders, such as panic attacks, hypochondria, dysthymias, phobias, undifferentiated somatoform disorders [8]. The conditions of the COVID-19 pandemic are likely to exacerbate mental disorders and cause an unsatisfactory response to ongoing therapy.

The various drugs that affect each of the pathogenetic links are used for the treatment of IBS [2]. Kolofort® is one of them. It produced on the basis of technologically processed antibodies. The affine purified antibodies to tumor necrosis factor α (TNF-α), to the brain-specific protein S-100 and to histamine are subjected to repeated sequential dilution with physical effects at each of the stages. Three active components in their combination have a complex effect on the central and peripheral links of the pathogenesis of functional disorders of the intestine [9].

The purpose of the observational study is to study the effectiveness of Kolofort® in patients with various variants of IBS that developed after COVID-19.

Materials and methods

The observational study included 32 outpatients with complaints abdominal pain, constipation, loose stools, flatulence, bloating, as well as anxiety and depression (Table 1). All of them had a history of COVID-19 pneumonia (with positive tests for SARS-CoV-2 RNA and 1–50 % of the lung involvement).

The dynamics of complaints was assessed by the FGID symptom questionnaire (Table 2), and anxiety by the Hamilton anxiety scale before and after treatment.

Kolofort® was prescribed to all patients in 2 tablets twice a day for 3 months.

The criteria for the effectiveness of Kolofort® was the changes in the scales for assessing symptom of IBS at the end of 1 month of therapy compared with the initial state.

The significance of changes in indicators was assessed using the Student's t-test with Statistica and MSExcel. The $\rho < 0.05$ level was accepted as a criterion of significance.

Results and discussion

We included 32 patients (10 men and 22 women). The age was 36.72 ± 5.90 years. Data on the clinical variant of IBS were reflected in Table 1.

Significant differences in the severity of IBS symptoms before and after therapy ($\rho < 0.05$) were observed on the scales: "abdominal pain decreasing after defecation", "violation of the consistency and / or frequency of stool", as well as "bloating (flatulence)" (Table 3).

The level of anxiety was significantly higher before treatment than after treatment (Table 4; $\rho < 0.05$), which may be due to a decrease in the severity of pain and discomfort in the abdomen disturbing the patient, normalization of the disturbed frequency and consistency of the stool, a decrease in flatulence during treatment with Kolofort®.

The results of prescribing Kolofort® in patients with IBS after COVID-19 are presented below in 2 clinical cases.

Patient 1, male, 38 years old, was hospitalised with coronavirus pneumonia in May 2021. The patient noted an increase in anxiety, a decrease in mood (hypothymia), impaired appetite and sleep during the hospitalization. A few days later thehospitalization,

Table 1. Distribution of patients taking into account the variant of IBS

	Number of patients with IBS (N = 32)	
Diagnosis	%	N
IBS with diarrhea	43,75	14
IBS with constipation	25,0	8
IBS, unclassified variant	21,875	7
IBS, mixed variant	9,375	3

Table 2. Questionnaire for the assessment of FGID symptoms

Have you had any symptoms during the previous week?	No	1 time per week	2–3 times a week	Daily	Several times a day
Pain in epigastrium					
Burning sensation in epigastrium					
Discomfort, heaviness and overflow in the abdomen after eating					
Early feeling of satiety					
Abdominal pain					
Bloating (flatulence)					
Violation of the consistency and / or frequency of the stool:					
- more often 3 times a day					
- liquid or mushy					
- less than 3 times a week					
- Solid or “sheep feces”					
The presence of a symptom: no — 0 points, 1 day a week — 1 point, 2–3 times a week — 2 points, daily — 3 points, several times a day — 4 points. When calculating the points reflecting the presence of a symptom should be summed up, the points obtained for each symptom should also be summed up.					
The sum of points before the start of treatment: __					
Total points after the end of treatment: __					

Table 3. Changes of the IBS symptom (M ± SD)

Name of the scale	Before treatment (N = 32)	After treatment (N = 32)	ρ
Abdominal pain	2,78 ± 0,63	1,875 ± 0,260	<0.05
Violation of the consistency and / or frequency of the stool	2,72 ± 0,49	1,625 ± 0,350	<0,05
Bloating (flatulence)	2,22 ± 0,58	1,31 ± 0,39	<0,05

diarrhea (semi-liquid stool 2–3 once a day) and flatulence developed. After discharge from the hospital, the severity of these symptoms increased and the patient called the doctor again.

Patient 2, female, 40 years old, had coronavirus pneumonia in September 2020 ans was treated at home. The patient from the moment she was informed about a positive PCR test for SARS-CoV-2 noted anxiety. Abdominal pain and diarrhea (loose stools, defecation 3 times a day) developed 2 days after it. The patient called the doctor again with complaints of abdominal discomfort, flatulence, diarrhea 3 times a day, as well as severe anxiety after COVID-19 recovery.

To exclude other diseases and confirm the functional nature of the disorder, both patients underwent a serological study for celiac disease, and the levels of fecal calprotectin, fecal lactoferrin and C-reactive protein were assessed in accordance with clinical guidelines for the diagnosis of IBS [2, 10]. These tests were negative.

These patients are prescribed a course of treatment with Kolofort® according to the standard scheme, 2 tablets twice a day for 3 months.

Table 4. Comparison of The Hamilton Anxiety Scale Before and After Koloforth® Treatment

	Before treatment (N = 32)		After treatment (N = 32)	
	%	N	%	N
No alarm (0–17 points)	18,75	6	53,13	17
Average severity of anxiety disorder (18–24 points)	59,38	19	43,75	14
Severe anxiety (25 or more points)	21,88	7	3,125	1

Table 5. Changes of indicators of the FGID symptom questionnaire in the clinical cases (in points)

Name of the scale	Before treatment (patient 1)	After treatment (patient 1)	Before treatment (patient 2)	After treatment (patient 2)
Violation of the consistency and / or frequency of the stool	8	0	7	0
Bloating (flatulence)	4	1	3	0

Table 6. Comparison of the Hamilton Anxiety Scale in the clinical cases

	Before treatment (patient 1)	After treatment (patient 1)	Before treatment (patient 2)	After treatment (patient 2)
No anxiety (0–17 points)	-	12	-	9
Average severity of anxiety disorder (18–24 points)	22	-	20	-
Severe anxiety (25 or more points)	-	-	-	-

Clinically significant changes during therapy were observed according to the questionnaire of symptoms of FGID on the scales "Violation of the consistency and/or frequency of stool" and "Bloating (flatulence)" (see Table 5).

Data on the level of anxiety in both patients with IBS before and after treatment with Kolofort® are reflected in Table 6.

Complex links in the pathogenesis of IBS require a complex therapeutic approach, which can be provided by the active components of Kolofort®. Anti-S-100 antibodies have a wide spectrum of psychotropic activity, including anxiolytic and antidepressant effects, which is clinically manifested, among other things, by a decrease in anxiety. Anti-TNHα antibodies have anti-inflammatory effect, and antibodies to histamine have antispasmodic effect [9].

The limitation of this study is the small number of patients examined, a limited period of observation, and the absence of the control group. This study was pilot and should encourage a randomized, placebo-controlled trial of Kolofort® in treatment of "post-Covid" IBS [7, 11]. The literature is gradually accumulating data on "post-Covid" IBS, and even more broadly on "post-Covid" FGID. Therefore, 6 months after COVID-19 in a group of 280 patients, 5.3 % developed IBS, 2.1 % — functional dyspepsia, 1.8 % — a combination of IBS and functional dyspepsia [12]. The search for the optimal drug approach remains relevant.

Conclusions

Kolofort® leads to a decrease in the symptoms of IBS and anxiety in patients who had COVID-19.

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