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CLINICAL GUIDELINES
Irritable bowel syndrome

Ivashkin V.T., Shelygin Yu.A., Baranskaya E.K., Achkasov S.I., Belous S.S., Belousova E.A., Beniashviili A.G., Vasiliev S.V., Grigoriev E.G., Kostenko N.V., Moskalev A.I., Kashnikov V.N., Loranskaya I.D., Lyashenko O.S., Poluektova E.A., Rumyantsev V.G., Timerbulatov V.M., Chashkova E.Yu., Shapina M.V., Sheptulin A.A., Shifrin O. S., Zolnikova O.Yu., Baranovsky A.Yu., Korochanskaya N.V., Mammaev S.N., Alekseeva O.P., Khlynov I.B., Tsukanov V.V., Alekseenko S.A.

ABBREVIATIONS

VHS — visceral hypersensitivity
GIT — gastrointestinal tract
RCT — randomized controlled trial
BOS — bacterial overgrowth syndrome
SSRIs — selective serotonin reuptake inhibitors
IBS — irritable bowel syndrome
IBS-D — irritable bowel syndrome with a predominance of diarrhea
IBS-C — irritable bowel syndrome with a predominance of constipation
IBS-M — irritable bowel syndrome, mixed type

TERMS AND DEFINITIONS

Irritable bowel syndrome (IBS) is a chronic functional bowel disease in which abdominal pain is associated with the defecation, changes in the frequency and nature of the stool.

1. BRIEF INFORMATION ON THE DISEASE OR CONDITION (GROUPS OF DISEASES OR CONDITIONS)

1.1 Definition of the Disease or Condition (Groups of Diseases or Conditions)

Irritable bowel syndrome (IBS) is a chronic functional bowel disease in which abdominal pain is associated with the defecation, changes in the frequency and nature of the stool.

1.2 Etiology and Pathogenesis of theDisease or Condition (Groups of Diseases or Conditions)

The etiology and pathogenesis of irritable bowel syndrome have been insufficiently studied. As one of the supposed links of pathogenesis, a violation of the structure and function of the muco-epithelial barrier of the gastrointestinal tract is considered, the cause of which is the polymorphism of genes responsible for the synthesis of its various components, acute intestinal infections, antibiotic therapy, changes in the composition of the microbiota, psycho-emotional stress and dietary features.

A change in the microbiota combined with a dysfunction of the muco-epithelial barrier leads to the formation of inflammatory changes in the intestinal wall. Chronic inflammation disrupts the mechanism of visceral sensitivity, which leads to hyperactivation of the higher nerve centers (primarily the limbic system) with increased efferent innervation of the intestine. This, in turn, leads to a spasm of smooth intestinal muscles and the formation of symptoms of the disease. Concomitant emotional disorders (anxiety, depression, somatization) contribute to the formation of a "vicious circle" in which the patient focuses on somatic symptoms, which further enhances them.

1.3 Epidemiology of theDisease or Condition (Groups of Diseases or Conditions)

IBS affects from 10 to 13% of the population. The proportion of people experiencing symptoms consistent with IBS is probably higher, but only 25–30% of them seek medical help. Women are more likely to suffer from this disease, and the diagnosis of IBS in most cases is established at the age of 30 to 50 years. In most patients with IBS

Table 1. *Bristol scale of form of feces*

Type 1	**separate hard lumps of feces (stool in the form of "nuts")**
Type 2	normal sausage-shaped feces, but with hard lumps
Type 3	feces are normal sausage-shaped, but with cracks in the surface
Type 4	feces of a normal sausage-shaped form or in the form of a snake with a smooth surface and a soft consistency
Type 5	feces in the form of soft blobs with clear-cut edges, easily evacuated
Type 6	pieces of feces with ragged edges, mushy consistency
Type 7	watery or entirely liquid stools with no solid pieces

(13–87%), the disease is combined with functional dyspepsia.

The presence of IBS is not accompanied by an increased risk of colorectal cancer or inflammatory bowel disease and an increased mortality. Despite the fact that IBS does not affect mortality, the disease can significantly impair the quality of life of patients [1] and leads to significant direct and indirect costs for its treatment and diagnosis [2].

1.4 Features of Coding theDisease or Condition (Groups of Diseases or Conditions) According to the International Static Classification of Diseases and Health-Related Problems

K58.0 Irritable bowel syndrome with diarrhea

K58.1 Irritable bowel syndrome with predominance of diarrhea

K58.2 Irritable bowel syndrome with predominance of constipation

K58.3 Irritable bowel syndrome with mixed bowel habits

K58.8 Other or unspecified irritable bowel syndrome

K58.9 Irritablebowel syndrome without diarrhea

1.5 Classification of theDisease or Condition (Groups of Diseases or Conditions)

Depending on the nature of the changes in the stool, four possible variants of IBS are distunguished: IBS with constipation, IBS with diarrhea, mixed and unclassified variants of IBS. This classification is based on the shape of the stool according to the Bristol scale, which is easily understood by patients and allows them to quickly identify the nature of stool disorders.

IBS with constipation (IBS-C): more than 25% of defecations, stool form is 1–2 on the Bristol stool scale; less than 25% of defecations — 6–7 on the Bristol stool scale. An alternative way to diagnose this type of the disease: the patient reports that he/she has predominantly constipation (type 1–2 on the Bristol stool scale).

IBS with diarrhea (IBS-D): more than 25% of defecations, the stool form is 6–7 on the Bristol stool scale, less than 25% of defecations — 1–2 on the Bristol stool scale. An alternative way to diagnose this type of the disease: the patient reports that he/she has predominantly diarrhea (type 6–7 on the Bristol stool scale).

Mixed type of IBS (IBS-M): more than 25% of defecations, the stool form is 1–2 on the Bristol stool scale, and more than 25% of defecations — 6–7 on the Bristol stool scale. An alternative way to diagnose this type of the disease: the patient reports that he/she has both constipation (more than in a quarter of all defecations) and diarrhea (more than in a quarter of all defecations). Respectively, type 1–2 and 6–7 on the Bristol stool scale.

Unclassifiable type of IBS (IBS-U): the patient's complaints correspond to the diagnostic criteria of IBS, but are insufficient for the first three types of the disease to be diagnosed.

It should be carefully evaluated patients' understanding of the terms "constipation" and "diarrhea". So many patients with IBS who complain of diarrhea mean frequent defecation, in which the stool remains formed; patients with

"constipation" may complain of discomfort in the anorectal region during defecation, and not infrequent movements or the passage of dense feces.

1.6 Clinical Picture of the Disease or Condition (Groups of Diseases or Conditions)

Complaints presented by patients with IBS can be conditionally divided into three groups:

- intestinal;
- related to other parts of the gastrointestinal tract (for example, nausea, heartburn) [3,4];
- non-gastroenterological (dyspareunia, feeling of incomplete emptying of the bladder, fibromyalgia, migraine) [5].

The presence of symptoms related to other parts of the gastrointestinal tract, as well as non-gastroenterological symptoms, makes the diagnosis of a functional disorder more likely. In addition, patients with IBS should be assessed for the presence of emotional disorders, such as anxiety, depressive or hypochondriac disorder [6,7].

Intestinal symptoms in IBS have a number of features.

Abdominal pain does not have a clear localization, but more often occurs in the left parts. The pain usually gets worse after eating. An important distinguishing feature of abdominal pain in IBS is its absence at night [8]. In women, the pain increases during menstruation [9].

The feeling of bloating is less expressed in the morning, increases during the day, increases after eating [10].

Diarrhea usually occurs in the morning, after breakfast, the frequency of stool varies from two to four or more times in a short period of time, often accompanied by imperative urges and a feeling of incomplete bowel emptying. Often, at the first act of defecation, the stool is denser than at subsequent ones, when the volume of intestinal contents is reduced, but the consistency is more liquid. The total daily weight of feces does not exceed 200 g. There is no diarrhea at night.

With constipation, it is possible to isolate "sheep" feces, feces in the form of a "pencil", as well as cork-like stools (the release of dense, formed feces at the beginning of defecation, then mushy or even watery feces). The stool does not contain amounts of blood and pus; however, an amount of mucus in the stool is often noted [11].

The clinical symptoms listed above cannot be considered specific for IBS, since they can also occur in other intestinal diseases.

When examining patients with IBS, attention is drawn to the discrepancy between the large number of complaints, the long course of the disease and the satisfactory general condition of the patient [11].

2. DIAGNOSIS OF THE DISEASE OR CONDITION (GROUPS OF DISEASES OR CONDITIONS). MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF DIAGNOSTIC METHODS

The diagnosis of IBS is established when the patient's complaints comply with Roman criteria IV, the exclusion of organic gastrointestinal diseases and the absence of "symptoms of anxiety".

According to Rome Criteria IV, irritable bowel syndrome (IBS) is defined as a functional bowel disease manifested by recurrent abdominal pain occurring at least once a week and characterized by the following signs (two or more):

1. Related to defecation;
2. Related to a change in the stool frequency;
3. Related to a change in the stool form.

These symptoms should be observed in the patient for the last 3 months with a total duration of at least 6 months.

As in the case of other functional diseases of the gastrointestinal tract, the diagnosis of IBS can be established based on the compliance of the patient's symptoms with the Roman criteria of the fourth revision in the absence of organic causes for their occurrence.

The "symptoms of anxiety" include the following symptoms, which may be a manifestation of an organic disease and should serve as an indication for an advanced examination.

Complaints and anamnesis:

- Body weightloss;
- Onset in an old age;
- Nocturnal symptoms;
- Colon cancer, celiac disease, ulcerative colitis and Crohn's disease in relatives;

- Constant abdominal pain as the only and leading symptom of gastrointestinal tract damage;
- Progressive course of the disease.

Direct examination:

- Fever;
- Changes from the internal organs (hepatomegaly, splenomegaly, etc.).

Laboratory indicators:

- Decrease in hemoglobin level;
- Leukocytosis;
- Increased ESR;
- The presence of occult blood in the feces;
- Changes in the biochemical analysis of blood;
- Steatorrhea and polyfecalia [11].

The Rome Criteria of the IV revision notes that a number of conditions, including chronic inflammatory bowel diseases, celiac disease, lactose and fructose intolerance, microscopic colitis, etc., can occur "under the mask" of IBS, and therefore, for the purpose of differential diagnosis, a limited range of studies can be conducted. According to the authors, the diagnosis of IBS should be based on four components: anamnesis of the disease, direct examination of the patient, minimal laboratory tests and (if there are clinical indications) the results of colonoscopy.

However, this approach is fraught with serious diagnostic errors, since a number of organic diseases, such as chronic inflammatory bowel diseases, microscopic colitis and even colon tumors, can occur with a clinical picture of IBS in the absence of "anxiety symptoms". Therefore, it is advisable to consider IBS as a diagnosis of exclusion.

2.1 Complaints and Anamnesis

Complaints and anamnesis typical for patients with IBS are indicated in subsection 1.6.

2.2 Physical Examination

Physical examination should be aimed at excluding organic disease and necessarily include examination of the perianal area and transrectal digital examination [5].

2.3 Laboratory Diagnostic Tests

It is recommended for all patients with a suspected diagnosis of IBS to conduct a general (clinical) blood test, a biochemical general therapeutic blood test to exclude changes characteristic of organic diseases (decreased hemoglobin level, leukocytosis, increased ESR, etc.) [12–14].

Category of recommendations — B (Level of evidence — 3)

It is recommended for patients with diarrheal and mixed variants of the disease to determine the content of antibodies to tissue transglutaminase in the blood (AT to tTG) IgA or, in case of selective IgA immunodeficiency, IgG to exclude celiac disease [15].

Category of recommendations — B (Level of evidence — 2)

It is recommended for all patients with suspected IBS to examine feces for occult blood to exclude organic diseases [11].

Category of recommendations — C (Level of evidence — 5)

It is recommended that patients with diarrheal and mixed variants of the disease conduct a stool examination in order to exclude the infectious nature of the disease [5,12,16].

Category of recommendations — B (Level of evidence — 3)

It is recommended for patients with diarrheal and mixed variants of the disease to conduct immunochromatographic rapid examination of feces for clostridium A and B toxins (Clostridium difficile) in order to exclude antibiotic-associated diarrhea and pseudomembranous colitis [17].

Category of recommendations — C (Level of evidence — 3)

It is recommended for patients with diarrheal and mixed variants of the disease to study the level of calprotectin in the feces to exclude inflammatory bowel diseases [14].

Category of recommendations — B (Level of evidence — 2)

2.4 Instrumental Diagnostic Tests

It is recommended that patients with diarrheal and mixed variants of the disease perform a hydrogen breath test with glucose or lactulose to detect the syndrome of excessive bacterial growth [18,19].

Category of recommendations — B (Level of evidence — 2)

It is recommended for patients with suspected IBS to conduct an ultrasound examination of the abdominal organs to exclude organic diseases [11].

Category of recommendations — C (Level of evidence — 5)

It is recommended that patients with suspected IBS undergo esophagogastroduodenoscopy to exclude organic diseases of the upper gastrointestinal tract [12, 20].

Category of recommendations — C (Level of evidence — 5)

Esophagogastroduodenoscopy with duodenal biopsy is recommended for patients with detected AT to tTG in the diagnostic titer or kinship or first-line relatives of patients with celiac disease to exclude celiac disease [15].

Category of recommendations — B (Level of evidence — 2)

It is recommended that all patients with IBS undergo ileocolonoscopy with a terminal biopsy of the terminal part of the small and large intestine to exclude organic diseases [12,21,22,25,26].

Category of recommendations — B (Level of evidence — 3)

2.5 Other Diagnostic Tests

Additional instrumental and laboratory tests are performed mainly for the purpose of differential diagnosis with a number of diseases.

- Lactase and disaccharidase deficiency, in which there is a connection between symptoms and the intake of certain products. Diagnosis is carried out using a respiratory hydrogen test with a load of lactose or fructose [23];
- Exocrine pancreatic insufficiency [24];
- Radiation (post-radiation) colitis;
- Colitis associated with nonsteroidal anti-inflammatory drugs;
- Ischemic disease of the digestive system;
- Colon cancer;
- Giardiasis [27];
- Diverticulitis [28, 29];
- Gynecological diseases (endometriosis, inflammatory diseases, ovarian tumors) [30–32].

Rare causes of the development of symptoms characteristic of IBS, primarily the diarrheal variant of the disease, include Whipple's disease, amyloidosis with intestinal lesion, as well as viral lesions of the colon (cytomegalovirus, herpes simplex virus).

3. TREATMENT, INCLUDING DRUG AND NON-DRUG THERAPY, DIET THERAPY, ANESTHESIA, MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF TREATMENT METHODS

3.1 Basic Principles of Therapy

The creation of a therapeutic union between a doctor and a patient includes a common view for the doctor and the patient on the nature of the symptoms of the disease and the diagnosis, an agreement on the treatment strategy (drug selection, waiting for the effect to form, patience when changing medications, adaptation to undesirable effects), an agreement on the boundaries of therapeutic resources [32].

3.2 Diet Therapy

The diet of patients with IBS should be selected individually by excluding products that cause increased symptoms of the disease (elimination diet). Despite contradictory research data on the assessment of the effect of prescribing a specific diet, all patients with IBS should be recommended:

- Eat regularly at a specially designated time, avoid eating in a hurry, while working;
- Do not skip meals and do not allow long breaks between them;
- It is advisable to recommend to the patient "keeping a food diary" to identify foods whose use leads to increased symptoms of the disease;
- Patients with diarrheal and mixed variants of IBS may be prescribed an aglutene diet [5].

The effectiveness of a diet low in oligo-di-monosaccharides (lactose, fructose, fructans, galactans) and polyols (sorbitol, xylitol, mannitol) [33] is doubtful [34,35].

Large-scale studies of the effectiveness of increasing physical activity in IBS have not been conducted.

Nevertheless, patients with IBS should be recommended moderate physical activity (walking, cycling, aerobics), which leads to a significant reduction in the main symptoms of the disease [36].

It is recommended for patients with IBS with insufficient effectiveness of the diet to prescribe alpha-galactosidase [37].

Category of recommendations — A (Level of evidence — 2)

3.3 Medication-assisted Treatment

Patients with IBS with complaints of abdominal pain are recommended to take antispasmodics to relieve pain syndrome [38].

Category of recommendations — A (Level of evidence — 1)

Comments. *The effectiveness of this group of drugs in comparison with placebo (58% and 46%, respectively) was confirmed in a meta-analysis of 29 studies in which 2,333 patients participated.*

The NNT index (the number of patients who need to be treated in order to achieve a positive result in one patient) when using antispasmodics turned out to be 7 [38].

When comparing the drugs, high efficacy was noted with the use of hyoscinabutyl bromide and pinaverium bromide (NNT = 3) [39]; in addition, according to some studies, the prescribing of some antispasmodics (for example, mebeverin**), along with a decrease in abdominal pain, leads to a significant improvement in the quality of life of patients with various IBS variants [40]. Mebeverin** also has a high safety profile and is well tolerated with prolonged use [41].

In general, according to various authors, the level of studies that confirmed the effectiveness of this group of drugs ranges from 1 to 3, the level of practical recommendations ranges from category A to C [42].

Patients with IBS are recommended to prescribe loperamide** to relieve diarrhea [43].

Category of recommendations — B (Level of evidence — 3)

Comments. *By reducing the tone and motility of the smooth muscles of the gastrointestinal tract, loperamide** improves the consistency of the stool, reduces the number of urges to defecate, however, does not significantly affect other symptoms of IBS, including abdominal pain. Due to the lack of randomized clinical trials (RCTs) in comparison of loperamide** with other antidiarrheal agents, the level of evidence of the effectiveness of taking loperamide ** belongs to category 2, the level of practical recommendations is attributed by some authors to category A, some to category C [39].*

Patients with IBS with diarrhea are recommended to prescribesmectitadioctahedral** to relieve diarrhea [44].

Category of recommendations — B (Level of evidence — 2)

Comments. *A randomized placebo-controlled study by Chang, F.Y. and co-authors (2007) evaluated the effectiveness of smectitadioctahedral** for 8 weeks in 104 patients with diarrheal IBS. Daily intake of the drug (1 sachet 3 times a day) contributed significantly (compared with the data at the initial stage of the study and placebo) to improving the quality of life of patients with IBS, as well as reducing the intensity of abdominal pain and flatulence [44].*

Patients with IBS with diarrhea are recommended to prescribe rifaximin to relieve diarrhea [45].

Category of recommendations — A (Level of evidence — 1)

Comments. *According to a meta-analysis of 18 randomized placebo-controlled trials involving 1,803 IBS patients with diarrhea, a short course of taking the non-absorbable antibiotic rifaximin effectively relieves diarrhea, and also helps to reduce bloating in such patients. At the same time, the NNT indicator turned out to be 10.2.*

Patients with IBS are recommended to prescribe antidiarrheal drugs of biological origin that regulate the balance of intestinal microflora or biologically active food additives (dietary supplements), probiotics, to relieve abdominal pain, normalize the frequency and consistency of stool [46–48].

Category of recommendations — A (Level of evidence — 2)

Comments. *Probiotics (A07F: Antidiarrheal microorganisms) are living microorganisms that benefit the host's health when administered in adequate quantities [49].*

A meta-analysis of 43 clinical trials that investigated the efficacy and safety of probiotics confirmed the positive effect of this group of drugs on the main symptoms of IBS [50]. The effectiveness of probiotics containing various strains of lacto- [51] and bifidumbacteria [52] has been proven.

A probiotic drug of proper quality must correspond to a number of requirements:

the shell containing the probiotic should ensure its unhindered passage through the gastrointestinal tract, followed by the delivery of a sufficient number of bacterial cells to the intestine; the probiotic drug should contain at least a billion (109) bacterial cells in a capsule or tablet at the time of sale and contribute to the destruction of pathogenic microorganisms

in the intestine, without adversely affecting other beneficial bacteria [53].

An alternative way is to preserve the viability of probiotics in the gastrointestinal tract and the delivery of microbial cells to the intestine by creating microcapsulated probiotic drugs [54].

*In the Russian Federation,for the treatment of IBS patients a biologically active additive has been developed and been used, containing such active ingredients as Bifidobacterium bifidum** (at least 1x109 CFU), Bifidobacterium longum (at least 1x109 CFU), Bifidobacterium infantis (at least 1x109 CFU), Lactobacillus rhamnosus (at least 1x109 CFU), as well as inactive ingredients (such as microcrystalline cellulose, calcium stearate, lactose), and meeting all the requirements for probiotic drugs. This BAA was approved by the Russian Gastroenterological Association (RGA).*

The effectiveness of the drug in terms of abdominal pain relief, normalization of stool frequency and consistency has been proven in randomized, placebo-controlled trials [46–48].

Patients with IBS with constipation are recommended to prescribe laxatives that increase the volume of intestinal contents for the treatment of constipation [39,55].

Category of recommendations — A (Level of evidence — 2)

Comments. *Drugs of this group increase the volume of intestinal contents, give fecal masses a soft consistency. They do not have an irritative effect on the intestine, are not absorbed, and are not addictive.*

According to the data of a 12-week randomized placebo-controlled trial, which included 275 patients, the prescribing of plantain oval seed shell at a dose of 10 g / day led to a significant decrease in the symptoms of the disease already during the first month of treatment; while on the background of the inclusion of bran in the diet (10 g/day), relief of the symptoms of the disease was noted only by the third month of follow-up, while the number of patients who refused to participate in the trial due to increased intensity of symptoms was significantly large in the group receiving bran [55].

In general, despite a fairly long period of use of dietary fiber in the treatment of IBS, their effectiveness remains ambiguous.

The prescribing of plantain oval seed shell leads to a significant decrease in the severity of symptoms of the disease, whereas insoluble dietary fiber (bran) is less effective and can lead to increased symptoms [39].

Patients with IBS with constipation are recommended to prescribe osmotic laxatives for the treatment of constipation [56, 57].

Category of recommendations — C (Level of evidence — 5)

Comments. *Osmotic laxatives. The most studied representatives of this group of drugs include polyethylene glycol (PEG, macrogol**), lactulose** and lactitol, which help slow down the absorption of water and increase the volume of intestinal contents.*

They are not metabolized in the gastrointestinal tract, do not cause structural changes in the colon and addiction, contribute to the restoration of natural urge to defecate.

The effectiveness of osmotic laxatives has been proven in randomized placebo-controlled trials, including long-term use (12 months) and the use in pediatrics. An increase in the frequency and improvement of stool consistency three months after the onset of treatment was observed in 52% of patients with IBS with a predominance of constipation while taking PEG and only in 11% of patients taking placebo. International clinical trials have shown the possibility of long-term use of PEG (up to 17 months) [56]. With the course prescribing PEG, the aftereffect was shown — ensuring the normal functioning of the intestine after the drug was discontinued. According to the American College of Gastroenterology (ACG) and the conclusion of the American Society of Colon and Rectal Surgeons (ASCRS), the level of evidence of the effectiveness of this group of drugs is 1, however, the category of practical recommendations varies from category A (according to ACG) to category B (according to ASCRS).

Taking into account the significant contribution to the regulation of gastrointestinal motility by the intestinal microbiota, which contributes to the formation of fecal masses and the production of various metabolites, primarily short-chain fat acids (SCFA), it is possible to prescribe drugs with a complex mechanism of action, having a normalizing effect on both gastrointestinal motility and the composition and functions of the intestinal microbiota (for example, lactitol) [57,58].

Patients with IBS with constipation are recommended to prescribe contact laxatives for the treatment of constipation [59].

Category of recommendations — A (Level of evidence — 2)

Comments. *Medications of this group stimulate chemoreceptors of the colon mucosa and enhance its peristalsis. According to the results of the trial, the number of independent acts of defecation in patients with chronic constipation while taking bisacodil ** increased from 0.9 to 3.4 per week, which was significantly higher than in patients taking placebo (an increase in the number of acts of defecation from 1.1 to 1.7 per week) [59].*

However, despite a fairly high level of efficacy and safety of this group of drugs, most of the trials conducted to determine these indicators were performed more than 10 years ago and can be classified as category 2 in terms of evidence. According to ACG data, the level of practical recommendations belongs to category B while according to ASCRS — C, which is probably due to the possibility of pain while taking stimulant laxatives [60].

According to the recommendations of the Russian Gastroenterological Association (RGA), the duration of treatment with drugs of this group should not exceed 10–14 days.

In patients with IBS, in the absence of an effect on the background of taking the above laxatives, prescribing of prucalopride is recommended [34, 62].

Category of recommendations — C (Level of evidence — 5)

Comments. *Prucalopride has been approved since 2009 in European countries for the treatment of chronic constipation in women, including in the obstetric variant of IBS, when laxatives did not provide the proper effect in eliminating the symptoms of constipation [32,61].*

Prucalopride has a positive effect on all symptoms of constipation, including concomitant (bloating, abdominal pain), and also improves the quality of life and provides a lasting effect with prolonged use. The drug is distinguished by the convenience of taking and dosing (1 mg in persons over 65 years of age or 2 mg in persons under 65 years of age once a day) and the predictability of the effect. Side effects of the drug, usually mild severity (headache, nausea, diarrhea, abdominal pain), are noted most often on the 1st day of treatment, in most cases they pass independently and do not require withdrawal of the drug. With the exception of the first day of administration, the tolerability of prucalopride is identical to placebo [62].

Patients with IBS are recommended to prescribe-trimebutin to reduce abdominal pain, normalize the frequency and consistency of stool [63–66].

Category of recommendations — B (Level of evidence — 2)

Comments. *In addition to drugs that affect any particular symptom of the disease — abdominal pain, diarrhea or constipation, medications are also used in the treatment of IBS patients, which, taking into account the mechanism of their action, contribute both reducing abdominal pain and normalizing the frequency and consistency of stool.*

Thus, for the treatment of abdominal pain and stool disorders in patients suffering from IBS, synthetic cholinoblockers are successfully used — esters with a tertiary amino group, normalizing intestinal motor activity, and, in addition, increasing the threshold of pain sensitivity due to exposure to glutamate receptors of the synapses of the posterior horns of the spinal cord [63]. The drug of this group, trimebutin, is safe for long-term use, and is also effective for the treatment of combined functional diseases (in particular, with a combination of functional dyspepsia syndrome and IBS [64]. The level of evidence of the effectiveness of the use of trimebutin corresponds to category 2, the level of practical recommendations corresponds to category B. According to the results of clinical trials, the treatment regimens, including trimebutine, demonstrate greater effectiveness compared to the regimens, including antispasmodics, in reducing the severity of symptoms of IBS and functional dyspepsia (according to the Questionnaire "7x7" [65]), with the exception of constipation and violation of the consistency of stool (hard stool) — in relation to these symptoms, the effectiveness of regimens with trimebutin was comparable to that in regimens with antispasmodics [66].

Patients with IBS are recommended to prescribeI-berogast to reduce abdominal pain, normalize the frequency and consistency of stool [67–69].

Category of recommendations — C (Level of evidence — 5)

Comments. *The drugs of plant origin and of combined action include Iberogast, obtained by alcohol extraction from nine medicinal plants (bitter Iberian, medicinal angelica, pharmacy chamomile, cumin, milk thistle, lemon balm, peppermint, celandine, licorice root).*

Iberogast is one of the most studied herbal medicines with proven efficacy [67,68].

In experimental and clinical trials, a multi-purpose (multi-target) effect of Iberogast has been established, consisting in normalization of motility of various parts of the gastrointestinal tract, reduction of visceral sensitivity and increased gas formation, anti-inflammatory and antioxidant effects [69]. According to the results of randomized placebo-controlled trials, in patients with IBS, Iberogast effectively reduces the severity of symptoms of the disease (abdominal pain, diarrhea, constipation).

The frequency of adverse events according to the studies of more than 46,000 patients did not exceed 0.04% [67]. With a presumptive diagnosis of functional dyspepsia and irritable bowel syndrome, as well as their combination, Iberogast can be prescribed immediately, before receiving the results of a full examination, to reduce the severity of symptoms [62].

Patients with IBS are recommended to prescribe Colofort to reduce abdominal pain, normalize the frequency and consistency of stool [70–72].

Category of recommendations — C (Level of evidence — 3)

Comments. *This drug has antispasmodic, anti-inflammatory and anxiolytic effects.*

The efficacy of the drug has been proven in randomized placebo-controlled trials [70–72].

The course of treatment is 1–3 months; if necessary, the course of treatment can be extended to 6 months and/or repeated after 1–2 months. On the background of an exacerbation of the disease, it is possible to increase the frequency of admission up to 4 times a day for a period of up to 14 days. The drug is used both as a monotherapy and in combination with antispasmodics and other medications.

Patients with IBS may be prescribed medications that normalize the permeability of the muco-epithelial barrier.

Comments. *As a result of the conducted trials, data were obtained on an increase in the permeability of the gastrointestinal muco-epithelial barrier and the significant role of these changes in the formation of symptoms in patients with IBS, which may in the future serve as a justification for prescribing drugs that normalize it.*

Patients with IBS are recommended to prescribe antidepressants to reduce abdominal pain [73,74].

Category of recommendations — A (Level of evidence — 1)

Comments. *The pathogenesis of IBS is quite complicated to formulate a universal hypothesis that could describe the nature of this disease.*

Publications from different years provide data on violations of the central mechanisms of pain sensitivity and regulation of intestinal motility, concomitant mental and behavioral disorders from the groups of mood disorders, anxiety and somatoform disorders [75–79].

Stress, mental traumatic events of the past often turn out to be significant factors for the development of IBS [73,74].

The circumstances described above explain the interest in a group of psychopharmacological drugs with a wide range of pharmacodynamic effects of central and peripheral properties [77].

Psychotropic drugs (nonselective monoamine reuptake inhibitors, selective serotonin reuptake inhibitors (SSRIs), as well as psycholeptics) are used to correct emotional disorders diagnosed in most patients suffering from IBS [6], as well as to reduce abdominal pain [5]. According to the meta-analysis, 12 randomized controlled trials (799 patients) conducted to evaluate the effectiveness of antidepressants in patients suffering from IBS, prescribing drugs of this group leads to a decrease in the severity of the main symptoms. At the same time, the well-being of patients receiving nonselective monoamine reuptake inhibitors was significantly better compared to the baseline level, while in the group of people receiving SSRIs, the differences were not significant [73]. Similar data on the low effectiveness of SSRIs are also given in earlier publications [74]. However, according to the Rome Criteria of the IV revision, antidepressants such as #paroxetine 10–40 mg per day; #sertraline 25–100 mg per day; #citalopram 10–40 mg per day can be prescribed to reduce abdominal pain [5]. Antidepressants are considered as fairly safe drugs in the treatment of IBS. When prescribing nonselective monoamine reuptake inhibitors, side effects such as dry mouth, drowsiness,

palpitations may occur; when prescribing SSRIs — sleep disturbance, headache, nausea and anxiety. In randomized placebo-controlled trials, the presence of side effects did not lead to a significantly more frequent need for withdrawal of antidepressants in comparison with placebo [73].

Patients with IBS are recommended to prescribe neuroleptics to reduce abdominal pain [78,80].

Category of recommendations — B (Level of evidence — 3)

Comments. *To date, neuroleptics (antipsychotics) in comparison with antidepressants have been less studied in patients with IBS.*

The successful use of some antipsychotic drugs to relieve symptoms of anxiety, depression, and autonomic dysfunction opens up the prospect of prescribing this group of medications for certain forms of IBS, when a clinically significant concomitant mental disorder can lead to increased severity of gastroenterological symptoms [78,80]. Along with the effect on comorbid mental disorders (81% of IBS patients have clinically significant manifestations of anxiety and/or depressive disorder [6]), psychopharmacological drugs have effects significant for the pathogenesis of IBS. For example, the blockade of histamine receptors of type 1 is important for the relief of pain sensitivity [74]; pronounced in some psychotropic drugs (neuroleptics, non-selective monoamine reuptake inhibitors) antispasmodic cholinolytic atropine-like activity — for the relief of muscle spasm [81]; the ability to interact with various subtypes of peripheral serotonin receptors can also make a significant contribution to the relief of IBS symptoms (change in stool frequency) [77].

3.4 Other Treatment

When evaluating psychotherapeutic techniques, it turned out that cognitive behavioral therapy (NNT = 3), hypnotherapy (NNT = 4), multicomponent psychotherapy (NNT = 4), when conducting the technique over the phone — NNT = 5, dynamic psychotherapy (NNT = 3.5) were successful.

There was no significant improvement in the well-being of patients during relaxation therapy, cognitive behavioral psychotherapy, behavioral psychotherapy conducted online, psychotherapy aimed at managing stress factors, meditative psychotherapeutic practices. However, in general, the evidence base for the effectiveness and presence of side effects of these techniques is insufficient [39].

4. MEDICAL REHABILITATION, MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF REHABILITATION METHOD

There are no specific rehabilitation measures for patients with IBS. Being a chronic disease associated with a number of emotional disorders, in most cases, with a long course of IBS, psychological (psychotherapeutic) counseling on the correction of risk factors for the development of non-communicable diseases is advisable, primary [65]. According to a systematic review, cognitive behavioral therapy [67–69], hypnotherapy [70] and psychological support [71–73] are effective in IBS.

5. PREVENTION AND DISPENSARY OBSERVATION, MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF PREVENTION METHODS

There are no specific IBS prevention measures. Being a benign disease that does not increase the risk of organic gastrointestinal diseases, IBS does not require additional routine follow-up and control examinations. The decision to re-examine is made individually when new symptoms appear, first of all, symptoms of anxiety, as well as when the course of the disease is resistant to therapy.

6. ORGANIZATION OF MEDICAL CARE

Medical care, with the exception of medical care within the framework of clinical testing, in accordance with Federal Law No. 323-FL of 21.11.2011 (ed. of 47 25.05.2019) "On the basics of protecting the health of citizens in the Russian Federation", is organized and provided:

1) In accordance with the regulation on the organization of medical care by type of medical care, which is approved by the authorized federal executive authority;
2) In accordance with the procedures for providing assistance in the profiles of "gastroenterology", "coloproctology", mandatory for execution on the territory of the Russian Federation by all medical organizations;
3) Based on the present clinical recommendations;

4) Taking into account the standards of medical care approved by the authorized federal executive authority.

Primary specialized medical and sanitary care is provided by a gastroenterologist, a coloproctologist and other specialist doctors in medical organizations licensed to provide appropriate types of medical activities. In case of suspicion or detection of IBS in a patient, internists, district internists, general practitioners (family doctors), specialist doctors, secondary medical workers, in accordance with the established procedure, refer the patient for consultation to a medical organization that has an office of a gastroenterologist, a coloproctologist, an outpatient gastroenterology center (unit), an outpatient coloproctology center (unit) to provide him/her with primary specialized medical care. Consultation in the specified structural units of the medical organization must be carried out no later than 30 working days from the date of issuance of the referral for consultation. A gastroenterologist, a coloproctologist of a medical organization that includes a consulting room of a gastroenterologist, a coloproctologist, an outpatient gastroenterology center (unit), an outpatient coloproctology center (unit), organize the performance of diagnostic tests necessary to establish a diagnosis. If it is impossible to perform diagnostic tests necessary to establish a diagnosis, as well as if there are indications for providing medical care in inpatient conditions, the patient is referred by the attending physician to the gastroenterology unit, coloproctology unit or other medical organization providing inpatient medical care to patients in the profile of "gastroenterology", "coloproctology". A gastroenterologist, a coloproctologist of a medical organization that has a consulting room of a gastroenterologist, a coloproctologist, an outpatient gastroenterology center (unit), an outpatient coloproctology center (unit) directs the patient to medical organizations, having a gastroenterology unit and/or a coloproctology unit in their structure for the provision of medical care in inpatient conditions to clarify the diagnosis (in case it is impossible to establish a diagnosis during the provision of primary specialized medical care) and the provision of specialized medical care. The deadline for the start of specialized medical care is determined by the decision of the commission for the selection of patients for hospitalization. The period should not exceed 30 calendar days from the date of issuance of the referral for hospitalization. Specialized medical care for IBS is provided by gastroenterologists, coloproctologists in medical organizations that have a gastroenterology unit and/or coloproctology unit, have a license, the necessary material and technical base, certified specialists, in inpatient and day hospital conditions and includes prevention, diagnosis, treatment of IBS, as well as medical rehabilitation. Indications for hospitalization in a 24-hour or day hospital of a medical organization providing specialized medical care for IBS are determined by a consultation of gastroenterologists and/or coloproctologists, with the involvement of other specialist doctors, if necessary. The indication for hospitalization to a medical organization in a planned form is:

1) The need to perform complicated interventional diagnostic medical interventions that require follow-up in a 24-hour or day hospital;
2) The presence of indications for specialized treatment of IBS, requiring observation in a 24-hour or day hospital.

The indication for the patient's discharge from the medical organization is:

1) Completion of a course of treatment or one of the stages of specialized medical care, in a 24-hour or day hospital, provided that there are no complications of treatment requiring medical correction and/or medical interventions in a hospital setting;
2) Refusal of the patient or his legal representative from specialized medical care in a 24-hour or day hospital, established by the council of the medical organization providing IBS treatment, provided there are no complications of the underlying disease and/or treatment requiring medical correction and/or medical interventions in inpatient conditions;
3) The need to transfer the patient to another medical organization according to the appropriate profile of medical care.

The conclusion on the expediency of transferring the patient to a specialized medical organization is carried out after a preliminary consultation on the provided medical documents and/or a preliminary examination of the patient by doctors-specialists

of the medical organization to which the transfer is planned.

7. ADDITIONAL INFORMATION (INCLUDING FACTORS AFFECTING THE OUTCOME OF THE DISEASE OR CONDITION)

The available data on the prognosis of the course of IBS are ambiguous. According to the most extensive study, in the majority of patients with IBS, symptoms, despite the treatment, persist, but do not worsen [75]. The probability of relief of IBS symptoms when observed for 12–20 months is 38%. Factors that have a negative impact on the prognosis of the disease include unwillingness to receive treatment, anxiety about the risks associated with the disease, disruption of daily functions as a result of IBS, a long history of IBS, chronic stress, as well as the presence of concomitant psychiatric diseases.

Table 2. *Criteria for assessing the quality of medical care*

№	Quality criteria	Level of evidence	Category of recommendations
1.	Ileocolonoscopy performed (yes/no)	2	B
2.	Antispasmodics are prescribed (yes/no)	1	A
3.	With IBS with a predominance of diarrhea, loperamide, and/or dioctahedral smectite, and/or rifaximin, and/or antidiarrheal drugs of biological origin regulating the balance of intestinal microflora or biologically active food additives (dietary supplements) are prescribed	1-2	A-B
4.	In the case of IBS with a predominance of constipation, laxatives and/or prucaloprid are prescribed	1	A

Scope of the Recommendations

These clinical recommendations are applicable in the implementation of medical activities within the framework of the Procedure for providing medical care to adults with diseases of the gastroenterological profile, as well as within the Procedure for providing medical care to people with diseases of the colon, anal canal and perineum of the coloproctological profile.

The Target Audience of these Clinical Recommendations

1. Therapeutists
2. General practitioners (family doctors)
3. Gastroenterologists
4. Coloproctologists
5. Health care organizers
6. Medical experts of medical insurance organizations (including during medical and economic expertise).

There is no conflict of interests.

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