REVIEW ARTICLE

Recent advances in the treatment of irritable bowel syndrome

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ABSTRACT

Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder which presents with abdominal pain and altered bowel habits. It affects about 20% of the general population, mainly women, and has a considerable impact on the quality of life and health care costs. Four different entities of IBS have been identified: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), IBS with a mixed pattern of constipation and diarrhea, and unclassified IBS. Although the precise pathogenesis of IBS remains unclear, its multifactorial nature is evident and includes environmental and host factors. Management of patients with this disease is challenging and a personalized approach is required. A strong, reassuring physician-patient relationship is crucial, followed by patient education, dietary advice, and stress reduction. For nonresponding patients, the therapeutic approach may include nonpharmacological therapies and/or pharmacotherapy. The choice of pharmacological treatment is based on the predominant symptom and a prespecified time point should be planned for effectiveness evaluation and dose adjustment. In patients with IBS-D, the therapeutic options include mainly antibiotics, such as rifaximin, peripheral opioid agonists, mixed opioid agonists/antagonists, bile acid sequestrants, and antagonists of serotonin 5-hydroxytryptamine type 3 receptors. Bulking agents and osmotic laxatives represent the first-line therapy for IBS-C, while lubiprostone and linaclotide should be reserved for difficult-to-treat patients. The involvement of gastrointestinal microbiota constitutes a fascinating field of exploration as it offers the potential to be modulated by the use of probiotics, prebiotics, synbiotics as well as fecal microbiota transplantation. This review offers an updated overview on the recent advances in the treatment of IBS.

Introduction Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder, affecting 9% to 16% of the general population, with a slightly higher incidence in women.[1] Its clinical presentation is characterized by abdominal pain associated with a change in stool frequency or form,[2] in the absence of organic disease. Depending on the predominant pattern of altered bowel habits, the Rome IV criteria divided IBS into 4 different entities: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), IBS with a mixed pattern of constipation and diarrhea (IBS-M), and unclassified IBS.[2] These subgroups are reflected by stool appearance, evaluated according to the Bristol Stool Form (BSF) scale, on days with at least one abnormal bowel movement. In IBS-D, at least 25% of bowel movements present with BSF 6 or 7 and less than 25% are BSF 1 or 2, while in IBS-C, at least 25% of bowel movements present with BSF 1 or 2 and less than 25% are BSF 6 or 7.[2] In IBS-M, more than 25% of bowel movements can be classified as BSF 1 or 2 and more than 25% are BSF 6 or 7, whereas patients with unclassified IBS meet the criteria for IBS, but the pattern of their bowel movements cannot be assigned into any of the previous 3 categories.[2]

Despite the relatively high prevalence of IBS and its relevance in terms of public health costs, its diagnosis and treatment are still challenging and require a strong physician-patient relationship.[3] Clinical management of patients with IBS requires both pharmacological and

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nonpharmacological approaches and should be based on the prevalent symptomatology. In this review, we will discuss the recent therapeutic advances and pathogenetic backgrounds of the 3 main symptoms of IBS: diarrhea, constipation, and abdominal pain.

Pathogenesis of irritable bowel syndrome

The pathogenesis of IBS is related to both host factors and environmental agents. Nevertheless, the precise mechanisms remain unclear.

Irritable bowel syndrome is traditionally considered part of the so-called "brain-gut disorders," along with other functional gastrointestinal diseases.[4] Connections between the central nervous system and myenteric plexus constitute the brain-gut axis: through this pathway, emotions can influence intestinal motility, mucosal secretion, and barrier function and, vice versa, mental function can be influenced by gastrointestinal stimuli.[5] It has been reported that patients with IBS have abnormal serotonin and dopamine secretion and both the degree and proportion of these alterations may play a role in determining the clinical pattern of the disease.[6]

Some patients with IBS, particularly those in the IBS-D subgroup, show an increased intestinal membrane permeability and hypersensitivity to somatic and visceral stimuli, leading to altered perception of pain.[7,8] Another factor involved in the pathogenesis of IBS is intestinal dismotility, which is related to dysregulation of the 5-hydroxytryptamine (HT) pathway. In fact, plasma levels of 5-HT are increased in patients with IBS-D and decreased in those with IBS-C.[3,9] This mechanism represents a target for pharmacological treatment with 5-HT4 receptor agonists, which act as prokinetic agents, or 5-HT3 receptor antagonists, which slow intestinal transit.

With regard to intestinal microbiota, their role in the pathogenesis of IBS is still not well defined, even though they are probably involved in barrier function alteration and mucosal inflammation.[10,11] Although many studies tried to characterize the composition of gut microbiota in patients with IBS,[10-12] the findings concerning its alterations vary significantly, probably depending on diet and geographic areas.[10] Moreover, despite the fact that small intestine bacterial overgrowth is prevalent in IBS, the causal and temporal relationship between these 2 conditions remains unclear.[3]

Environmental factors involved in the pathogenesis of IBS include psychosocial distress, infections, antibiotic use, diet, and food intolerance.[3] The important role of psychosocial factors is reflected by the association between IBS and psychological disorders (anxiety and depression).[13,14] In fact, gastrointestinal symptoms are exacerbated by psychological distress and, conversely, abdominal pain and changes in bowel habits can intensify symptoms of anxiety and depression.[13]

Approximately 10% of patients who develop IBS have a previous history of enteric infections[3] and 3% to 36% of cases of gastroenteritis are followed by persistent IBS symptoms.[15] This could be related to mucosal inflammation, alterations in mucosal immunity and enteric nervous system as well as to gut microbiota modification.[16] Moreover, even though food allergies among patients with IBS are rare,[17] intolerances are quite common, and poorly absorbed carbohydrates can increase bowel fermentation, thus triggering IBS symptoms in individuals with gut hypersensitivity.[3]

Since IBS is characterized by complex and multifactorial pathogenesis, the diagnosis requires a stepwise approach with exclusion of organic disease and fulfillment of the Rome IV criteria, which define IBS as recurrent abdominal pain, occurring at least once a week in the preceding 3 months, related with defecation or associated with a change in the frequency or form of stools. The onset of symptoms must occur at least 6 months before the diagnosis.[2] Exclusion of an organic cause of symptoms requires careful taking of medical history and physical examination, with special attention to alarm symptoms, which include blood in the stools, anemia, unintentional weight loss, fever, nocturnal symptoms, and symptom onset after the age of 50 years. Colonoscopy should be reserved for patients presenting with the abovementioned manifestations or those with a family history of colorectal cancer,[3,18] while in other cases, only a few noninvasive diagnostic tests are needed.[3] In order to exclude anemia or inflammation, a complete blood count as well as measurement of plasma C-reactive protein levels and fecal calprotectin should be performed. Moreover, in patients with diarrhea, fecal analysis, serology for celiac disease, and thyroid function tests are indicated.[3] In specific cases, breath test for lactose malabsorption or a dietary exclusion trial can be considered.[18] Finally, as bile acid malabsorption can be found in more than a quarter of IBS patients with diarrhea,[19] a scintigraphic evaluation to rule out bile acid malabsorption or a therapeutic test with a bile acid–binding agent, which is less expensive and more feasible, can be useful diagnostic options in these individuals.[3,18]

Once IBS is diagnosed, identification of the subtype can guide the treatment. The therapeutic approach in IBS is not standardized; it should be individualized and targeted on the main symptoms (TABLE 1).[20]

Nonpharmacological treatment

Lifestyle interventions

Lifestyle interventions, such as dietary modifications, physical activity, and stress reduction represent the most important nonpharmacological clinical approach for patients with IBS.

The recently published British Society of Gastroenterology guidelines highlight that dietary advice should be considered a first-line approach, with strong recommendation and weak quality of evidence.[21] The traditional dietary advice recommended by the National Institute for Health and Care Excellence for patients with IBS include

TABLE 1 Treatments for irritable bowel syndrome depending on the subtype of the disease (modified from Adriani et al[3])

Pharmacotherapy for diarrhea	
Peripheral opioid agonist	Loperamide (2–4 mg/d up to 16 mg/d)
Bile acid sequestrants	• Cholestyramine (9 g twice or thrice daily) • Colestipol (2 g once or twice daily) • Colesevelam (625 mg once or twice daily)
5-HT3 receptor antagonists	• Alosetron (0.5–1 mg twice daily) • Ondansetron (4–8 mg thrice daily) • Ramosetron (5 mg once daily)
Mixed opioid agonists/antagonists	Eluxadoline (100 mg twice daily)
Antibiotics	Rifaximin (550 mg thrice daily for 14 d)
Pharmacotherapy for constipation	
Soluble fiber	Psyllium (up to 30 g/d in divided doses)
Laxatives	Polyethylene glycol (17–34 g/d)
Type 2 chloride-channel activator	Lubiprostone (8 μg twice daily)
Guanylate cyclase-C agonist	Linaclotide (290 μg once daily)
Pharmacotherapy for abdominal pain	
Antispasmodics	• Dicycylomine (10–20 mg once daily) • Otilonium (40–80 mg twice or thrice daily) • Mebeverine (135 mg thrice daily) • Peppermint oil (250–750 mg, twice or thrice daily)
Peripheral opioid agonists	Trimebutine (150 mg twice or thrice daily)
Tricyclic antidepressants	• Desipramine (25–100 mg/d) • Amitriptyline (10–50 mg/d)
Selective serotonin reuptake inhibitors	• Paroxetine (10–40 mg/d) • Sertraline (25–100 mg/d)
Nonpharmacological treatment	
Lifestyle interventions	• Dietary modifications • Physical activity • Stress reduction
Microbiome manipulation	• Probiotics, prebiotics, and synbiotics • Fecal microbiota transplantation
Complementary and alternative medicine	• Relaxation training • Hypnotherapy • Cognitive-behavioral therapy • Acupuncture

a regular meal pattern, with avoidance of large meals or skipping meals, liquid intake of almost 2 liters a day, with limited consumption of alcohol or fizzy drinks, and reduced intake of fat, insoluble fibers, caffeine, and gas-producing food such as fresh fruit.[22]

Elimination diets may relieve symptoms of IBS, while skipping meals has demonstrated to worsen them.[23] Increase in the intake of fiber is a useful therapeutic option for patients with IBS-C; however, insoluble fiber, such as wheat bran, can worsen flatulence and abdominal pain.[3,24] Hence, soluble fiber should be preferred, initially at a low-dose (3–4 g/day) and built up gradually to avoid bloating.[21] Fat intake has shown to worsen diarrhea in patients with IBS-D and increased carbohydrate intake is correlated with exacerbation of IBS symptoms.[15] Fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs), such as fructans, galactans, lactose, fructose, sorbitol, xylitol, and mannitol can induce bowel fermentation, thus increasing pain and flatulence.[3,15] Dietary restriction of FODMAPs (a so-called low-FODMAP diet [LFD]) could relieve these symptoms,[25] even though the superiority of this approach to the traditional IBS diet is uncertain.[26] A recent prospective randomized controlled trial (RCT) including 166 patients with IBS-D compared traditional dietary advice with a strict LFD followed by systematic reintroduction of FODMAPs (a "modified" FODMAP diet). Both groups showed an improvement of IBS symptoms and quality of life scores, but this amelioration was significantly more pronounced in the LFD group.[27] Currently, LFD is recommended as a second-line dietary approach.[21]

Patients with IBS can experience worsening of symptoms after intake of lactose or gluten. The role of lactose intolerance in IBS is controversial[3]: compared to the general population, patients with IBS more often report symptoms related to lactose malabsorption, despite similar rates of hydrogen positivity on breath test.[28] However, in some IBS patients, decreased intake of lactose can alleviate symptoms, probably because of both reduced gas production and gut distention.[29] Similarly, some patients experience abdominal symptoms following gluten ingestion in the absence of celiac disease.[3] This clinical manifestation could be attributed to poorly absorbable carbohydrates rather than gluten itself or to nonceliac gluten sensitivity.[30] Further studies are needed to clarify the relationship between gluten ingestion and IBS symptoms.

Complementary and alternative medicine could play a role in nonpharmacological treatment of IBS, even though currently available data provide conflicting evidence regarding its efficacy. Considering the influence of psychosocial factors on clinical manifestations of IBS, relaxation training, hypnotherapy, and cognitive-behavioral therapy may be beneficial to IBS patients[3,15]; their application, however, is limited by considerable costs and prolonged duration as well as by poor patient and clinician acceptance.[3] Acupuncture can act on serotonergic and cholinergic pathways, thus influencing the brain-gut axis.[15] Some RCTs have investigated its effect on IBS symptoms[31] and a meta-analysis including 17 studies showed no evidence of the superiority of acupuncture to sham acupuncture in terms of symptom control or quality of life.[31] Finally, Chinese herbal treatments were shown to be effective in symptom control, with no statistical difference when compared with traditional therapy based on antispasmodics.[32] However, the former were associated with a significantly higher rate of adverse events, such as gastrointestinal symptoms, skin rash, and elevated levels of liver enzymes.[32]

Probiotics, prebiotics, and synbiotics The potential role of microbiota manipulation in IBS has been receiving increasing attention. Probiotics, prebiotics, and synbiotics are widely used in patients

with IBS, while fecal microbiota transplantation (FMT) is an emerging treatment whose application is being studied.

Probiotics are living nonpathogenetic microorganisms which, when administered in adequate amounts, have a positive effect on the host's health.[33] Probiotic products may contain a single strain or a combination of 2 or more strains and their effect is strain-specific and cannot be generalized.

Prebiotics are nondigestible disaccharides or oligosaccharides, such as inulin and (trans) galacto-oligosaccharides, which modulate the composition and activity of intestinal microbiota, thus beneficially affecting the host's health.[33,34] Probiotics and prebiotics can be combined in synbiotics, in which the prebiotic compounds selectively favor the probiotic microorganisms, with a synergic action.[33] The beneficial effect of these compounds in IBS is attributable to different mechanisms, such as reduction of low-grade inflammation, gut motility regulation, modulation of bile salt metabolism, and reduction of the number of competing pathogens through production of antimicrobial substances and interfering in intestinal mucosal adhesion.[34] Some combinations of probiotics and prebiotics were shown to reduce symptoms of IBS in small therapeutic trials. For example, in a case-control study including 37 patients with IBS there was a significant improvement of abdominal pain, abdominal distention, and stool consistency in patients treated with a combination of L-tryptophan, inulin, angelica, vegetal charcoal, vitamin PP, B-group vitamins (B_1, B_2, B_6), and probiotics (*Lactobacillus sporogenes*, *Lactobacillus acidophilus*, *Streptococcus thermophilus*).[35] Two subsequent meta-analyses demonstrated limited evidence for the efficacy of prebiotics or synbiotics in IBS.[36,37] However, the use of *Lactobacillus plantarum DSM 9843*, *Escherichia coli DSM17 252*, and *Streptococcus faecium* resulted in a significant reduction in global symptoms of IBS.[36] Nevertheless, the wide variability of the administered compounds and the different scales for symptom evaluation limit the possibility to draw general conclusions on the efficacy of these treatments. The recent guidelines on IBS management suggest to try this approach for 12 weeks and discontinue in case of lack of improvement (level of recommendation, weak; quality of evidence, very low).[21]

As far as FMT is concerned, it is currently approved for resistant *Clostridium difficile* infection, in which it was shown to be an effective therapy,[38] while its application in IBS has shown conflicting results. In an RCT including 90 patients with IBS-D or IBS-M, FMT performed in 55 patients through colonoscopy showed a significant clinical efficacy compared with placebo.[39] These results were confirmed by subsequent smaller studies.[40-42] However, another RCT, involving 52 IBS patients who received active FMT or placebo capsules for 12 months did not show beneficial effects favoring FMT.[43] A subsequent meta-analysis including 8 single-arm trials and 5 RCTs demonstrated that while FMT proved to have a significant clinical benefit in the former, in RCTs it did not show superiority to placebo.[44] In light of these controversial results, the efficacy and safety of FMT in IBS should be further evaluated through studies including larger and more homogenous samples.

Pharmacological treatment **Irritable bowel syndrome with diarrhea** The therapeutic options for IBS-D include antibiotics (such as rifaximin), peripheral opioid agonists, mixed opioid agonists / antagonists, bile acid sequestrants, and antagonists of serotonin 5-HT3 receptors.

Rifaximin is a nonabsorbable rifamycin, which was shown to significantly reduce global IBS symptoms, bloating, and loose or watery stools after 2 weeks of treatment. It has good tolerability, as the incidence of adverse events associated with its use is not superior to that of placebo.[45] Furthermore, this drug was demonstrated to be safe and effective also in repeated treatments of recurrent symptoms.[46]

Loperamide is a peripheral agonist of μ-opioid receptor, often used as first-line treatment of diarrhea in IBS-D, as it inhibits peristalsis and reduces fecal volume.[3] It can be used both in chronic diarrhea and in case of intermittent symptoms, on an as-needed basis. Despite its efficacy in reducing the frequency of bowel movements and improving stool consistency, loperamide did not improve global IBS symptoms or abdominal pain. The latter, on the contrary, could be a side effect of this drug. Moreover, it should be used with caution in patients with mixed symptoms because of the risk of severe constipation.[15] Eluxadoline is a mixed μ-opioid agonist and δ-opioid antagonist. Similarly to loperamide, it slows bowel motility by acting on μ receptors, while the δ-receptor antagonism allows a reduction of visceral pain. Constipation and nausea represent main side effects of this drug; however, a small proportion of patients reported more serious adverse events, such as sphincter of Oddi dysfunction or self-limited pancreatitis. Therefore, eluxadoline is contraindicated in patients with a history of pancreatitis, bile duct obstruction, sphincter of Oddi dysfunction, or alcohol abuse.[47]

Bile acid sequestrants, such as cholestyramine, colestipol, and colesevelam, are a useful therapeutic option for IBS-D, especially in patients with bile acid malabsorption, who represent more than a quarter of this group.[19] They were shown to improve stool consistency and decrease the frequency of bowel movements. The main limitations of bile acid sequestrants are interference with the absorption of other drugs[47] and the risk of constipation, which can be avoided by appropriate dose modification (starting with a low dose and gradually increasing it).[3]

Antagonists of serotonin 5-HT3 receptors, such as alosetron, ondansetron, and ramosetron, were

originally developed for chemotherapy-induced nausea, but they were also shown to slow colonic transit time.[3] In particular, alosetron proved to be effective in alleviation of abdominal pain, improvement of stool frequency and consistency, and higher quality of life scores in IBS-D patients.[48-50] Possible side effects include ischemic colitis and constipation; therefore, 5-HT3 antagonists should be prescribed only in selected patients, starting with low doses.[3-47]

Irritable bowel syndrome with constipation Bulking agents and osmotic laxatives represent the first-line therapy for IBS-C. Soluble fiber supplementation with psyllium and ispaghula was shown to improve global symptoms in patients with IBS-C,[13,15] while insoluble fiber, such as wheat bran, did not show efficacy in symptom improvement; conversely, it could exacerbate flatulence and abdominal pain.[3,24] Polyethylene glycol is an osmotic laxative which was shown to be superior to placebo in terms of constipation improvement with good tolerability, the same effect was not demonstrated for abdominal pain relief.[50]

Agonists of serotonin receptors 5-HT4 act as prokinetic agents, thus improving gastrointestinal motility. Nevertheless, the use of cisapride and tegaserod is limited by the risk of adverse cardiac events, such as arrhythmias and ischemic cardiac events. Prucalopride has not been associated with adverse cardiovascular events, probably because of its high selectivity for 5-HT4 receptors.[51] Even though its efficacy has not been evaluated in patients with IBS,[3] prucalopride was shown to be effective in chronic idiopathic constipation[52] and it represents a useful therapeutic option in case of laxative failure.

Lubiprostone is a prostaglandin derivative which selectively activates type 2 chloride channel, thus stimulating intestinal fluid secretion.[13] It was demonstrated to be significantly superior to placebo in improving constipation and global IBS symptoms, with a modest effect on abdominal pain and a favorable safety profile.[53] Linaclotide increases intestinal chloride secretion through the cystic fibrosis transmembrane regulator by acting on guanylate cyclase-C.[3] In phase 3 trials, it was shown to significantly improve both bowel movements and abdominal pain[54,55]; its main side effect was diarrhea, which was reported by almost 20% of patients.[13] Furthermore, a recent systematic review and network meta-analysis has shown that among the licensed drugs, linaclotide was the most efficacious at relieving abdominal bloating, a troublesome symptom that often occurs in patients with IBS-C.[56]

Irritable bowel syndrome with a mixed pattern of constipation and diarrhea Irritable bowel syndrome with a mixed pattern of constipation and diarrhea represents a diagnostic and therapeutic challenge, as no drug has been specifically studied for patients with this type of IBS. Moreover, the mixed bowel pattern could be due to an underlying disease or a medical intervention itself. Therefore, a detailed history-taking, including prescribed drugs or over-the-counter medications and supplements, is necessary to exclude the possible causes of alternating bowel habits.[57] Most patients with IBS-M experience periods with a reduced frequency of bowel movements and small, hard stools, alternating with periods of multiple stools of variable consistency. In some cases, this is a result of progressive stool accumulation during the periods of constipation, culminating in bowel purging.[57]

The therapeutic approach for these patients is based on the same pharmacological options as described above for diarrhea and constipation, and needs real-time adaptations in order to fit the patient's symptoms. In case of constipation, bulking agents or osmotic laxatives should be prescribed, starting with low doses and titrated according to the stool consistency and frequency. Similarly, in periods with diarrhea, the dosage of loperamide or bile acid sequestrants should be carefully modulated as they can cause constipation.

Pharmacotherapy for abdominal pain Abdominal pain is often associated with either IBS-D, IBS-C, or IBS-M and it is related to visceral hypersensitivity, abnormal contractility of gastrointestinal muscular layer, and gut distension.

Antispasmodic drugs reduce gastrointestinal contractility through anticholinergic mechanism (dicyclomine) or calcium channel blocking (otilonium, mebeverine).[3] Their efficacy in improving symptoms of IBS, both in monotherapy or in combination with simethicone, has been analyzed in several trials. Even if the methodology of these studies is not homogeneous, a meta-analysis showed that antispasmodic agents are superior to placebo in the treatment of IBS, with good tolerability.[58] Also, peppermint oil acts as an antispasmodic through calcium channel blocking and it was shown to be more effective than placebo in relieving IBS symptoms and abdominal pain.[3] Trimebutine (3,4,5-trimethoxybenzoic acid 2-[dimethylamino]-2-phenylbutylester) is a peripheral agonist of μ, k, and δ opioid receptors and modulates the release of gastrointestinal peptides such as motilin, vasoactive intestinal peptide, gastrin, and glucagon.[3] Trimebutine accelerates gastric emptying and modulates gut contractility; it was also shown to decrease reflexes induced by gut distension in animal models. In patients with IBS and other functional gastrointestinal disorders, trimebutine proved to be superior to placebo in the treatment of both acute and chronic abdominal pain.[59]

In case of chronic abdominal pain, a good response may be achieved through antidepressants,[15] as they enhance endogenous endorphin release, promote activation of descending inhibitory pain pathways through norepinephrine antagonism, and regulate the neuromodulating effect of serotonin.[15] Moreover, central-acting agents were demonstrated to have therapeutic

effects unrelated to mood improvement, as they can modify gastrointestinal motility.[60] The choice of the most appropriate antidepressant should be guided by the prevalent IBS pattern: in case of diarrhea, tricyclics antidepressants should be preferred,[60] while in constipation, selective serotonin reuptake inhibitors may be useful because of their prokinetic effect.[3] Similarly to psychological treatments, however, the use of antidepressants can be limited by social stigma and poor patient acceptance.

Due to their modulating effect on the autonomic nervous system, dorsal vagal nuclei, and enteric nervous system, benzodiazepines may play a role in the treatment of IBS, especially in visceral pain management, even though few studies have analyzed their efficacy.[61] In patients with IBS-D or IBS-M, dextofisopam was demonstrated to improve stool consistency in both men and women; however, stool frequency was reduced only in women and no effect on bloating, partial defecation, or hospital anxiety and depression scale scores was observed.[62] Therefore, both dextofisopam and other benzodiazepines need further evaluation to assess their possible clinical benefit in patients with IBS.

Conclusions Irritable bowel syndrome is a common disorder with significant impact on public health and patients' quality of life. Its diagnosis requires the exclusion of organic disease through careful taking of medical history, physical examination, and selected diagnostic tests. The treatment of IBS is still challenging, as it requires a strong physician-patient relationship and an individualized approach focused on the main symptom. In patients with IBS-D, the available pharmacological therapies include antibiotics, peripheral opioid agonists, bile acid sequestrants, mixed opioid agonists / antagonists, and antagonists of serotonin 5-HT3 receptors. On the other hand, in case of constipation, bulking agents and osmotic laxatives represent the first-line therapy, whereas further therapeutic options include prokinetics and drugs stimulating intestinal fluid secretion, such as lubiprostone and linaclotide. The treatment of acute or chronic pain may also be challenging. Antispasmodics and trimebutine were shown to be effective in relieving acute abdominal pain, but in case of chronic pain, central-acting agents, such as antidepressants, may be a better choice. Together with these pharmacological therapies, dietary modifications and increased physical activity should be encouraged. Dietary interventions include increased intake of soluble fibers in IBS-C as well as reduced consumption of fat and insoluble fibers and a regular meal pattern with avoidance of meal skipping or large meals. Beside the traditional dietary advice, restriction of FODMAPs has shown promising results in improving symptoms and quality of life in IBS. Moreover, IBS patients can experience worsening of symptoms after lactose or gluten intake, but the relationship between IBS and lactose malabsorption or nonceliac gluten sensitivity is still unknown. The role of fecal microbiome in IBS has been receiving increasing attention: probiotics, prebiotics, and synbiotics are a widely used therapeutic option, while FMT is an emerging treatment, which has shown controversial results and therefore needs further evaluation. Other nonpharmacological interventions include alternative medicine such as hypnotherapy, acupuncture, herbal remedies, or relaxation techniques. However, so far there has been little evidence in terms of the efficacy of these approaches in the treatment of IBS symptoms.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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