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Current knowledge on irritable bowel syndrome treatment - literature overview

Authors:

Ilona Jasiuk [IJ]
Independent Public Clinical Hospital No.1 in Lublin, Stanisława Staszica 16, 20-400 Lublin, Poland
ilona.jasiuk@gmail.com
https://orcid.org/0009-0009-8544-3276

Kamil Chrościński [KC]
Independent Public Clinical Hospital No.1 in Lublin, Stanisława Staszica 16, 20-400 Lublin, Poland
kamilchr@onet.pl
https://orcid.org/0009-0000-0468-7901

Ewa Łukaszewska [EŁ]
VOXEL NZOZ MCD, ul. Paderewskiego 5, 37-100 Łańcut, Poland
lukaszewska.ewapaulina@gmail.com
https://orcid.org/0009-0000-6065-7213

Ilona Sajkiewicz [IS]
Stefan Wyszyński Specialist Hospital in Lublin, Kraśnicka 100, 20-718 Lublin, Poland
inasajka@gmail.com
https://orcid.org/0009-0007-5954-3594

Nadia Miga-Orczykowska [NMO]
Stefan Wyszyński Specialist Hospital in Lublin, Kraśnicka 100, 20-718 Lublin, Poland
nadmig98@gmail.com
https://orcid.org/0000-0002-0551-6159

Paulina Lemieszek [PL]
Stefan Wyszyński Specialist Hospital in Lublin, Kraśnicka 100, 20-718 Lublin, Poland
paulina.lemieszek13@gmail.com
https://orcid.org/0009-0001-6648-7283

Justyna Wójtowicz [JW]
Stefan Wyszyński Specialist Hospital in Lublin, Kraśnicka 100, 20-718 Lublin, Poland
wojtowicz.justtyna@gmail.com
https://orcid.org/0009-0006-6079-9637

Katarzyna Krukar [KK]
Provincial Combined Hospital in Kielce Grunwaldzka 45, 25-736 Kielce, Poland
kasiakrukar3@interia.pl
https://orcid.org/0009-0001-5544-8027

Martyna Pustelniak [MP]
Provincial Combined Hospital in Kielce Grunwaldzka 45, 25-736 Kielce, Poland
martyna.pustelniak@onet.pl
https://orcid.org/0009-0000-5606-0385
Klaudia Kister [KK]
1st Clinic of Psychiatry, Psychotherapy and Early Intervention, Medical University of Lublin
20-079 Lublin, Poland
klaudia2178@gmail.com
https://orcid.org/0000-0003-2058-5395

Jakub Laskowski [JL]
Department of General and Pediatric Ophthalmology, Medical University of Lublin, 20-079 Lublin, Poland
i.laskowski0609@gmail.com
https://orcid.org/0000-0002-9547-0608

Katarzyna Rudnicka [KR]
Stefan Wyszyński Provincial Specialist Hospital in Lublin, Aleja Krasnicka 100, 20-718 Lublin, Poland
katarzyna.rudnicka95@gmail.com
https://orcid.org/0009-0005-6815-6276

Abstract:

Introduction: Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by symptoms such as abdominal pain, bloating, and altered bowel habits. It affects a large proportion of the general population leading to a negative effect on the quality of life. The pathophysiology of IBS is not fully known. There are several therapies currently used in the treatment of IBS. They vary from changing dietary habits to antibiotic therapy and must be personalized.

Aim of the study: To review and summarize the current state of knowledge on the treatment of irritable bowel syndrome.

Methods and materials: This review was conducted based on available data published in the PubMed database, using the following phrases: "irritable bowel syndrome", „ibs", "treatment of ibs", and "FODMAP diet".
Conclusion: The treatment of irritable bowel syndrome remains a challenge. Each patient requires a personalized treatment. After a correct diagnosis of the IBS subtype, therapy should focus on the main symptoms such as bloating or diarrhea.

Keywords: Irritable Bowel Syndrome, gut-brain axis, FODMAP diet, chronic gastrointestinal disorder

1. Introduction

Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder affecting approximately 10% of the global population [1,2]. It is characterized by irregular bowel movements combined with abdominal discomfort or pain in the absence of detectable organic and biochemical abnormalities [3]. The pathogenesis of IBS is complex, with several theories explaining its symptoms: alterations in gut microbiota, psychological factors, and gut-brain axis disorders [4].

Depending on the predominant symptoms and stool appearance, the Rome IV criteria classify IBS into four main subtypes: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), mixed IBS (IBS-M), and unclassified IBS (IBS-U) [1]. The diagnosis of IBS subtypes varies geographically. In the United States, there is an equal distribution of diagnoses, whereas in Europe, IBS-C or IBS-M may be more prevalent [5]. The treatment of IBS depends on its subtype, and both pharmacological and non-pharmacological methods are used to alleviate symptoms. Due to the unknown pathogenesis and numerous factors affecting gut function, managing patients with IBS is challenging. The treatment process involves finding the best-individualized alternative for the patient, a task that is not easy [4,5].

2. Etiopathogenesis

The pathophysiology of IBS remains poorly understood. Pathogenic factors such as genetic predispositions, visceral hypersensitivity, food intolerance, altered gut-brain axis,

intestinal dysmotility, innate immune disturbances, and dysbiosis may contribute to this disorder. Additionally, changes caused by infections or bacterial overgrowth in the digestive system may initiate IBS. Physical or sexual abuse in childhood, a short period of breastfeeding, food allergies, overweight, or any surgical procedures may also influence the development of the disease [6,7,8]. Since symptoms vary among individuals, it remains unclear which pathogenic factors trigger or exacerbate IBS [6].

Diagnosis of IBS can be divided into four subtypes: IBS-D – with predominant diarrhea; IBS-C – with predominant constipation; IBS-M – mixed subtype; IBS-N – unclassified [7]. The diagnosis is based on the Rome IV criteria, which define IBS as a functional bowel disorder, where recurrent abdominal pain is associated with defecation or changes in bowel habits. Typically, there are disturbances in bowel habits (e.g., constipation, diarrhea, or a mix of both) as well as symptoms of bloating/abdominal tension. Symptoms should begin at least six months before diagnosis and be present for at least three months [21]. To exclude organic causes of symptoms, a thorough history and physical examination are necessary, with special attention to alarm symptoms [1].

3. Treatment

The therapeutic approach to IBS is not standardized. It should be individualized and focused on the main symptoms. Determining the IBS subtype helps guide the treatment process [1].

Probiotics

Probiotics contain single or mixed cultures of live bacteria that have been shown to improve health by modifying gut flora. They positively impact the intestinal mucosa through numerous processes, including reducing the growth and binding of harmful bacteria, strengthening epithelial barrier functions, and modulating the host's immune response. IBS patients may benefit from probiotics by reducing bloating, discomfort, and stool frequency [7]. Probiotics do not have serious side effects, and there is no significant difference in observed adverse events between probiotics and placebo [10]. Unfortunately, there are inherent difficulties in definitively establishing the role of gut microbiota in the pathophysiology of IBS due to the clinical heterogeneity of IBS and the limitations of available studies [9].

Prebiotics

Prebiotics are non-digestible substances that improve the growth of intestinal bacteria. Prebiotics include among others lactulose, galactooligosaccharides, oligosaccharides, xylo-oligosaccharides or soybean oligosaccharides such as inulin, pectin, cellulose, hemicellulose and starch. It is found naturally in food such as fruits, bananas, asparagus, cereals, tomatoes, artichokes, garlic, onions, olives, barley, celery, and wheat. In some cases, they are produced synthetically, such as lactulose, galactooligosaccharides, fructooligosaccharides, cyclodextrins, and lactose sucrose [28].

Some evidence-based RCTs (Randomized Controlled Trials) have been published with inulin, galactooligosaccharides, and fructooligosaccharides. They observed clinical improvement in global symptoms, bloating, and nausea in IBS patients, as well as changes in microbiota composition, including increased proportions of bifidobacteria and fatty acids. Shorter intestinal chains are associated with improved symptoms in IBS patients [29].

Fecal Microbiota Transplantation

Fecal microbiota transplantation (FMT), a microbiome-based therapy, has garnered significant scientific interest in recent years. FMT aims to restore balanced gut flora by infusing stool from healthy donors into the gastrointestinal tract of patients to treat specific conditions. This procedure involves administering a healthy stool solution to the recipient's digestive system [11]. A recent meta-analysis found that FMT administered via gastroscopy or a nasojejunal tube are effective method for treating IBS [12].

Diarrhea

Rifaximin

It is a non-systemic antibiotic indicated for treating adults with IBS-D, representing a short-term therapy [13]. The use of this drug is supported by clinical studies. Two identically designed phase 3, placebo-controlled studies evaluated the efficacy of rifaximin at 550 mg three times daily for two weeks in significantly alleviating overall symptoms, bloating, abdominal pain, and loose or watery stools [14]. Combined results from both studies showed that 40.8% of patients treated with rifaximin experienced significant improvements in

abdominal pain and stool consistency compared to 31.7% of placebo-treated patients. Serious adverse events associated with its use are rare [14,15].

Loperamide

It is an opioid receptor agonist that reduces peristalsis and fluid secretion, resulting in delayed bowel transit and reduced fluid and electrolyte loss. It significantly alleviates diarrhea symptoms but has not consistently been shown to improve overall IBS symptoms or abdominal pain. Adverse effects include abdominal pain, bloating, nausea, vomiting, and constipation [16].

Bile Acid Sequestrants

Cholestyramine is considered a second-line drug for IBS with predominant diarrhea. Some studies suggest that a significant number of patients with this IBS subtype may have mild or severe bile acid malabsorption. Bile acid sequestration can alleviate the choleretic effect in patients with idiopathic bile acid malabsorption. However, since bile acid malabsorption can result from rapid ileal transit, a simpler and more acceptable approach is to first use loperamide [1,17].

5-HT3 Receptor Antagonists (alosetron, ondansetron, and ramosetron)

Serotonin plays a crucial role in controlling gastrointestinal motility. High serotonin levels are observed in patients with IBS-D, while low serotonin levels are associated with IBS-C [6].

Constipation

For mild to moderate IBS-C symptoms, initial management tools should include dietary and lifestyle modifications. A randomized, placebo-controlled study compared the efficacy of increasing soluble (psyllium) or insoluble fiber (bran) in the diet of IBS patients. It was found that patients taking psyllium experienced significant improvements in symptoms relief and overall symptoms reduction, whereas bran showed no clinical benefits and often worsened symptoms [3]. Polyethylene glycol can be used in cases resistant to treatment, as it has been shown to improve stool frequency. It has not been shown to significantly reduce abdominal pain compared to placebo [18]. Linaclotide and lubiprostone are secretagogues recently used to treat IBS-C. A phase 3 randomized study found that 12-week treatment with linaclotide significantly improved IBS relief, spontaneous bowel movements, stool consistency, straining,

abdominal pain, discomfort, and bloating compared to placebo. Diarrhea was the most common adverse event, with a low discontinuation rate [19,20].

Diet

Food plays a dual role in IBS; it is a symptom trigger but also a therapy tool. Food and its breakdown products can affect various aspects of gut physiology, including motility, permeability, microbiome, gut-brain axis interactions, immune regulation, and neuroendocrine functions. A low FODMAP diet (monosaccharides, disaccharides, fermentable oligosaccharides and polyols) is frequently included in the initial treatment approach for IBS. Food containing these compounds includes stone fruits, grains, vegetables, dairy products, and artificial sweeteners. Gases produced by FODMAPs lead to bloating. The osmotic effect of FODMAPs also increases fluid inside the intestinal lumen, causing gastrointestinal distension and stimulating abnormal bowel motility [4,6]. If a low FODMAP diet is indicated, it should be implemented under the supervision of a dietitian and for the shortest possible period (e.g., 4 weeks) [16]. The modified NICE diet (small, frequent meals, avoiding symptom-triggering foods, and avoiding excess alcohol and caffeine) is another option for IBS patients and appears to have the same effect as a low FODMAP diet in some countries [4].

Wheat

One of the most controversial, but also interesting aspects of the IBS diet is the inclusion of wheat because it contains gluten, which is an allergen high in fructans and belongs to the group of fermentable carbohydrates [25]. There are five randomized controlled trials suggesting that IBS patients may benefit from a gluten-free diet. However, the available evidence suggests this solution is controversial [25, 26]. The results showed that gastrointestinal symptoms occurred significantly more frequently in the fructan group than in the gluten group. Similarly, there were no significant differences between the gluten group and the placebo group. Therefore, it can be concluded that the symptoms of IBS patients worsened after consuming fructans. This was not the case after including gluten in the diet [26].

Other medications

Antidepressants

Patients with chronic abdominal symptoms may respond to low doses of tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs) [5]. Commonly used TCAs include imipramine, desipramine, and amitriptyline, while SSRIs include fluoxetine, paroxetine, and escitalopram. Physicians are encouraged to use antidepressants in scenarios where patients have not responded to more conventional IBS therapies and also have coexisting mental health conditions [23]. Few studies report the use of serotonin-norepinephrine reuptake inhibitors (SNRIs) in the treatment of IBS [22].

Gabapentin/Pregabalin

Several small randomized controlled trials (RCTs) have been published regarding the use of this class of drugs in the treatment of irritable bowel syndrome (IBS). These studies indicate that gabapentin and pregabalin can significantly reduce urgency and improve bowel elimination in patients experiencing abdominal pain. However, the small sample sizes of these studies necessitate further research with larger populations to confirm these findings [33].

Clonidine

It is an alpha-2-adrenergic agonist that has been shown in some studies to reduce abdominal pain and overall improvement of IBS symptoms. However, its side effects, such as nausea, dry mouth, and diarrhea limit its use [27].

The benzodiazepines

They should be considered when treating patients with co-occurring anxiety disorders. Alprazolam or diazepam are used in other countries, either alone or in combination with anticonvulsants, but there are no RCTs (Randomized Controlled Trials) to support their use [33].

Ketotifen

It is a mast cell regulator. A randomized controlled trial (RCT) involving 60 patients demonstrated a significant reduction in abdominal pain and improved tolerance to rectal distension. The side effects, primarily drowsiness, were generally well tolerated [33, 34].

Psychotherapy

Although the physical symptoms are the most apparent, research shows that psychological factors play a crucial role in the course and severity of this condition. Therefore, psychotherapy can be an effective tool in supporting the treatment of IBS [24].

Cognitive-behavioral therapy (CBT)

Cognitive-behavioral therapy (CBT) is one of the most commonly used forms of psychotherapy for treating IBS. CBT helps patients identify and change negative thoughts and behaviors that may exacerbate their symptoms. This process includes learning stress management techniques, as stress is a common trigger for IBS symptoms. Patients also learn how to avoid catastrophizing and how to replace negative thinking patterns with more constructive ones. Studies have shown that CBT can significantly reduce IBS symptoms and improve patients' quality of life [30].

Hypnotherapy

Hypnotherapy is another psychotherapeutic approach that has proven effective in treating IBS. This therapy focuses on deep relaxation and suggestions aimed at reducing gut sensitivity and improving brain-gut communication. Patients often learn self-hypnosis techniques, which they can use at home to alleviate symptoms in everyday stressful situations. Hypnotherapy can also help patients build a positive attitude towards their health and manage their condition better [31].

Psychodynamic Therapy

Psychodynamic therapy focuses on exploring unconscious conflicts and emotions that may contribute to IBS symptoms. Working with a therapist helps patients understand how their past experiences impact their current health problems. Therapy can help uncover and work through difficult emotions, which may lead to a reduction in physical symptoms [9].

Stress Management

Stress is one of the main triggers for IBS symptoms. Many psychotherapeutic techniques, such as relaxation training, meditation, or mindfulness, can help patients manage stress. Regular practice of these techniques can not only alleviate IBS symptoms but also improve overall well-being and mental health [17].

Emotional Support

Psychotherapy also offers emotional support, which is crucial for IBS patients. Conversations with a therapist can help patients cope with feelings of helplessness, frustration, and anxiety that often accompany this condition. This support can also help patients build stronger relationships with their loved ones, which is an important aspect of recovery [5, 30].

In conclusion, psychotherapy plays a key role in treating Irritable Bowel Syndrome by offering tools for stress management, changing negative thinking patterns, and providing emotional support. With these techniques, patients can not only alleviate physical symptoms but also improve their quality of life [17].

The doctor-patient relationship (DPR)

The doctor-patient relationship (DPR) is very important for patients with IBS. Developing an optimal DPR is crucial for communication, and the doctor must convey several key points to the patient with IBS. This includes informing them that IBS is a real disease that affects the quality of life, that it is chronic and intermittent, and that while there is no "magic pill" to cure it, there are alternatives for long-term symptom control [32]. This allows for symptom verification, empathy towards the patient, and setting realistic expectations. It should also be explained that IBS does not cause cancer, does not shorten life expectancy and that stress can trigger symptoms. This reduces anxiety, encourages exploration of psychological factors, and emphasizes the need for a collaborative approach [19, 32].

4. Summary

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by symptoms such as abdominal pain, altered bowel habits and bloating. It affects a large portion

of the general population, negatively impacting the quality of life. The pathophysiology of IBS is not fully understood. After correctly diagnosing the IBS subtype, therapy should focus on the main symptom. There are many therapies currently used in the treatment of IBS, from dietary changes, and antibiotic therapy to psychotherapy. Treating irritable bowel syndrome remains challenging, and each patient requires personalized treatment.

Author's contribution:

Conceptualization, supervision, and project administration: Ilona Jasiuk, Kamil Chróściński, Ilona Sajkiewicz, Paulina Lemieszek, Katarzyna Krukar, Klaudia Kister

Methodology: Ewa Łukaszewska, Nadia Miga-Orczykowska, Justyna Wójtowicz, Martyna Pustelniak, Klaudia Kister, Katarzyna Rudnicka

Software, validation, formal analysis, investigation, resources, writing original draft preparation: Ilona Jasiuk, Kamil Chróściński, Ewa Łukaszewska, Justyna Wójtowicz, Martyna Pustelniak, Jakub Laskowski

Writing review editing and visualization: Ilona Sajkiewicz, Ewa Łukaszewska, Nadia Miga-Orczykowska, Paulina Lemieszek, Katarzyna Krukar, Jakub Laskowski, Katarzyna Rudnicka

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