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Irritable bowel syndrome: systematic review of origin, pathology, diagnosis and treatment

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Abstract

Irritable bowel syndrome is the most common problem of gastrointestinal practice worldwide. It contains group of symptoms that affect the gastrointestinal tract. People with IBS may experience abdominal pain, diarrhea, constipation, cramps.

It's still being under discussion whether the irritable bowel is a pathological or a psychological syndrome. People report various symptoms, so they also consult doctors of different medical specializations. For the same reason doctors may have problems with accurate diagnosis of IBS.

As evidenced by recent studies, IBS is associated with psychological distress and impaired quality of life. It's also important from economical and medical care system point of view - they utilize the health care system to a greater degree than patients without this diagnosis.
The aim of this review is to provide a comprehensive evidence-based review of the diagnosis, pathogenesis and treatment to guide clinicians diagnosing and treating their patients.

Materials and methods: The review was based on the analysis of materials collected in the „Pubmed" database, books and other scientific articles. The search was performed using the keywords: „IBS", „irritable bowel syndrome", „ibs diet", „rome criteria", „gut-brain axis", "causes of ibs", „low FODMAP"

Introducion

In 1892, Osler first described "mucous colitis" as a condition involving the passage of mucus and other substances from the colon, with patients typically having normal colonic lining but suffering from psychological issues and abdominal pain. Hurst also acknowledged this condition, but it vanished from medical practice and literature by the late 1920s. By 1928, the term "mucous colitis" was redefined to mean colonic spasm. The term "irritable colon" was introduced in 1929 by Jordan and Kiefer to describe a colonic musculoneural disturbance affecting many gastroenterology outpatients, characterized by abdominal pain and irregular bowel movements, which is similar to the current understanding of the condition.[1]

Materials and methods

The review was based on the analysis of materials collected in the „Pubmed" database, books and other scientific articles. The search was performed using the keywords: „IBS", „irritable bowel syndrome", „ibs diet", „rome criteria", „gut-brain axis", "causes of ibs", „low FODMAP"

Definition and epidemiology

According to World Gastroenterology Organization, about 9% to 23% of the global population suffer from IBS [2] Over the years, the definition of IBS has changed.

In general, IBS is characterized by abdominal pain or discomfort that is alleviated by defecation or begins with a change in stool frequency (either increasing or decreasing) or stool appearance (becoming loose or hard). The absence of alarming symptoms such as gastrointestinal bleeding, weight loss, fever, anemia, or an abdominal mass indicates IBS rather than a structural disease. Individuals with IBS may also experience comorbid conditions more frequently than expected, including gastro-esophageal reflux, genito-urinary symptoms, fibromyalgia, headaches, backaches, and psychological symptoms. As a result, IBS can present to various subspecialists and is often initially misdiagnosed.[3]

IBS can be categorized into those with predominantly diarrhea (IBS-D) or predominantly constipation (IBS-C). Some patients experience a mix of constipation and diarrhea, and it is possible for individuals to alternate between these patterns. Highly variable bowel signs and symptoms are indicative of IBS, however the presence of stomachache and disturbed defecation is crucial for diagnosis. According to the WHO DMS-IV code

classification, IBS can be classified as diarrhea-predominant, constipation-predominant, alternating stool pattern (IBS-A), or pain-predominant. In some cases, IBS may have an acute onset following an infectious illness, which includes symptoms like fever, vomiting, diarrhea, or a positive stool culture[4].

Population-based studies indicate that IBS is a very common condition. In Western countries like the United States and Australia, about 10% of the general population meets the Rome III criteria for IBS, though many never seek medical advice for it. IBS overlaps with other unexplained gastrointestinal symptoms, such as chronic constipation and dyspepsia, suggesting these conditions may share a common cause. In Western countries, IBS is more prevalent among females, a trend not observed in Eastern countries. It is believed that IBS is underdiagnosed in Asia and that its prevalence may rise due to changes in diet and infectious risk factors.[5]

Patophysiology

There are many hypotheses that potentially can contribute to IBS. Typically, IBS has been understood as a condition involving visceral hypersensitivity (causing abdominal discomfort or pain) and gastrointestinal motor disturbances (causing diarrhea or constipation). However, these motor disturbances, such as changes in intestinal transit, do not fully explain mixed or alternating IBS. Some believe these abnormalities may be secondary to psychological issues rather than primary causes. Nevertheless, not all IBS patients have significant psychological factors, and referral bias might influence the observed psychological associations. Emerging evidence suggests that organic diseases of the gastrointestinal tract can be identified in some patients who meet the Rome criteria for IBS. Increasing research points to subtle inflammatory bowel disease, serotonin dysregulation, bacterial overgrowth, and central dysregulation as potential factors. Although the exact causes of IBS are not yet fully understood, post-infectious IBS (IBS-PI) is a distinct entity, and a genetic contribution to IBS is also likely.

Additionally, research indicates a potential genetic contribution to IBS, although its significance is still debated. The search for candidate genes is ongoing, based on the hypothesis

that environmental factors play a crucial role in the development of IBS in genetically predisposed individuals.[6]

Although the correlation between IBS and immune activation is not clear these days, there is growing evidence suggesting that immune activation plays a role in the development of IBS, particularly in post-infectious IBS (IBS-PI).[7]

About 10% of IBS patients report their symptoms began following an infectious illness.

Recent research has also found an elevated innate immune response in IBS patients, indicated by the expression and activation of Toll-like receptors. Additionally, psychological stress is known to trigger immune activation, but it is unclear if immune activation in IBS patients is mainly due to infectious gastroenteritis or psychological stress[8].

Serotonin dysregulation is another factor, which can contribute to development of IBS symptoms[9]. Serotonin influences gastrointestinal motility, sensation, and secretion. Studies have shown that plasma 5-HT levels are decreased in IBS patients with constipation[10] but increased in those with diarrhea[11], particularly in those experiencing postprandial symptoms. This supports the idea that serotonin is involved in the motor and sensory dysfunctions seen in IBS. Consequently, serotonin receptors have become potential therapeutic targets for IBS: 5-HT4 receptor agonists are expected to enhance gastrointestinal propulsion (acting as prokinetics)[12], while 5-HT3 receptor antagonists are anticipated to slow gastrointestinal transit and reduce visceral sensation[13].

The next possible dimension which may play role in causing IBS is bacterial overgrowth (SIBO). Direct link between SIBO and IBS isn't firmly established, but there are some evidences that bacteria may contribute to some IBS symptoms[14].

The last trigger, which will be discuss in this paper is central dysregulation and brain-gut interaction.

Psychosocial factors seem to play a significant role in IBS, although whether they directly influence gastrointestinal function is uncertain. Conversely, gastrointestinal dysfunction might also affect central processes. Evidence suggests a link between childhood or adulthood abuse and IBS, although its etiological significance is debated[15]. Anxiety and

depression are commonly associated with IBS[16]. While some view IBS as a somatization disorder, the presence of organic pathophysiology in certain cases makes this unlikely[15].

The central nervous system regulates various functions such as secretion, motility, and blood flow[17]. Gut signals are involved in regulating reflexes, and perception of gut events involves activation of afferent pathways, modulated at both peripheral and central levels[18]. Functional magnetic resonance imaging has significantly advanced our understanding of brain-gut interaction in IBS, enabling the comparison of cortical function between healthy individuals and IBS patients [19]. Brain responses differ in IBS patients, with greater activation of certain brain regions like the anterior cingulate cortex, amygdala, and dorsomedial frontal cortex during rectal distention compared to patients with ulcerative colitis and controls[20]. It's hypothesized that non-IBS individuals have better activation of endogenous pain inhibition areas, potentially indicating a genetic predisposition to IBS. Amitriptyline, an antidepressant, has been shown to alleviate rectal pain by activating specific brain regions such as the right prefrontal cortex, right insula, and perigenual anterior cingulate cortex [21]. These central changes may explain the therapeutic effects of antidepressants in IBS.

Clinical presentation

The variety of symptoms, which occur in patients with IBS is commonly used for qualification to a specific subtype of the disease. The essential division consists of four main domains determined by abbreviations: IBS-C, IBS-D, IBS-M and IBS-U. In order they stay for conditions with prevalent constipation (more than 25% of stools described as 1 or 2 in the Bristol Stool Form Scale and less than 25% stools described as 6 or 7 in BSFS scale), diarrhea (the reverse of the aforementioned), their combination (over 25% constipation and over 25% diarrhea) and the absence of listed stool abnormalities. (Table 1)[22,23] The individual subgroups are willing to melt into other ones. Even though the bowel pattern is crucial for providing appropriate treatment, it does not strike the core of the problem.[24, 25]

The patients who present to a doctor and are eventually diagnosed with IBS complain mostly of recurrent, intermittent lower abdominal pain, changes in bowel movements and bloating. Abdominal pain usually does not awake patients but can be described as harassed and cramp-like. However, there are also some more subtle symptoms, which the patients can easily miss. They have been meticulously collected in many research and summarised by Ford and colleagues in their work. These symptoms include the presence of mucus per rectum,

incomplete evacuation, looser and more frequent stools at the onset of pain, pain relief by defecation, and visible abdominal distension.[26]

Apart from the gastrointestinal tract symptoms, there are also non-gastric manifestations. It is notable, that the majority of IBS patients are women between the age of 20-40 years old. Furthermore, there is a significant collocation between gastric symptoms and the prevalence of depression, mood disorders, oligomenorrhea, headache, fatigue, back pains and polyuria.[27]

Diagnosis

The foundation of diagnosis is an accurate dialogue with the patient followed by physical examination as IBS can be easily mistaken with other diseases and do not possess any pathognomonic symptom or lab test. The questions about family cancer or autoimmunology disease history, diet, unintentional weight loss and presence of blood in stool should be posed.[22] Depending on the collected information, the clinicians ought to run a limited number of tests, which among others include complete blood count, guaiac stool test, fecal calprotectin level, erythrocyte sedimentation rate, C-reactive protein level or even endoscopy with biopsies or imaging. In some cases the doctors should also run thyroid tests and celiac antibody levels.[28,29] It is worth emphasizing that these tests are not crucial for IBS diagnosis, their role is limited to other diseases' rejection. They should not be conducted without specific reason resulting from patient's examination.[27]

Multiple criteria have been created since 20th century to put the entire knowledge of IBS in order and simplify diagnostic process. As of this moment the most widespread criteria remain the Rome IV criteria, which was released in 2016. They include recurrent abdominal pain which happens at least once a week within 3 months observations. The pain must relate to defecation, change of defecation incidence and shift in stool consistency. According to the Rome IV criteria nothing less than two associations should be achieved.[30]

Differential Diagnosis

As we have mentioned, there are no guidelines, that dictate performing any lab tests before making a diagnosis of IBS. It should mainly be based on Rome IV criteria. A diagnostic approach focused on symptoms was compared to one that involved ruling out organic diseases through extensive blood tests, stool analysis, and flexible sigmoidoscopy with biopsies. Both

methods showed no difference in quality of life or patient satisfaction, but the symptom-based approach was less costly. Nevertheless, if there are any suspicious of organic causes of symptoms, they should be run out with the aid of appropriate tests.

Clinicians frequently order a complete blood count and measure C-reactive protein to help exclude the possibility of inflammatory bowel disease. According to guidelines for managing celiac disease, people showing symptoms like IBS should undergo serologic testing for celiac disease. This recommendation is supported by a meta-analysis, which discovered that patients with any type of IBS had a significantly higher rate of biopsy-confirmed celiac disease compared to those who did not have IBS.[31]

For postmenopausal women who have recently started experiencing constipation overlap with lower abdominal pain and bloating, it is possible to perform a pelvic and rectal examination. If a solid is detected, both abdominal and transvaginal ultrasounds should be conducted, as these symptoms, though uncommon, could be indicative of ovarian cancer.[32]

For IBS-D and IBS-M subtypes, measuring fecal calprotectin levels is beneficial, as it effectively distinguishes between IBS and IBD with high sensitivity and specificity.[33] Moreover, certain biomarkers, like colonic transit rates or levels of fecal bile acids, could help identify different mechanistic subtypes of IBS. This could lead to more personalized and targeted therapies for individuals with the condition.

Treatment

LOW FODMAP DIET

This diet involves restricting fructose, oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP). These substances are poorly absorbed, which may lead to a feeling of flatulence due to the osmotic reaction and fermentation in the large intestine. Foods containing FODMAP include fruits, vegetables, grains, nuts, and dairy products. Unfortunately, research does not clearly determine the clinical benefits of using this diet in patients with IBS. Nevertheless, the current guidelines of the British Dietetic Association recommend a low FODMAP diet as a second-line treatment for IBS.[34,35]

FIBER

The clinical effects of fiber treatment depend on its type and daily intake. Insoluble fibers are not effective in alleviating IBS symptoms. Among all types of soluble fibers, soluble viscous low fermentable fibers are the most effective in reducing symptoms such as bloating, flatulence, abdominal distention, and increasing fecal weight. An example of such fiber is psyllium, which particularly relieves the symptoms of IBS-C and IBS-D. 25 g for women and 38 g for men is a recommended daily intake of soluble fibers.[35]

GLUTEN-FREE DIET

Some patients with IBS experience gastrointestinal and extra-intestinal symptoms after consuming gluten. If celiac disease and wheat allergy have been excluded in these patients, non-celiac gluten sensitivity can be diagnosed. The most common symptoms are abdominal pain and flatulence. There may be a justification for recommending a gluten-free diet to carefully selected patients with functional abdominal bloating or distension, particularly those who report symptoms related to gluten. Unfortunately, there are no studies confirming the effectiveness of a gluten-free diet in patients with IBS and non-celiac gluten sensitivity.[36]

PROBIOTICS

Probiotics offer several positive physiological benefits in the gut, making them suitable for use as a therapy for IBS. They modulate gut microbiota, prevent pathogens from adhering to the gut lining, enhance the gut barrier function of the mucosa by reducing low-grade immune activation, increasing the mucus layer, and producing tight junction proteins. They also possess anti-inflammatory effects by suppressing proinflammatory cytokines.[37] Unfortunately, research conducted on the effectiveness of probiotics in the treatment of IBS provide inconsistent results. Studies have been conducted comparing the effects of using mono- and multi-strain probiotics and the general observation is that a multi-strain probiotic supplement can potentially alleviate IBS symptoms. However, the particular symptoms improved by probiotic supplementation varied across different studies.[38]

PSYCHOLOGICAL THERAPIES

Multiple studies have shown positive correlations between psychological distress and the worsening of gastrointestinal symptoms that trigger IBS. There are therapies that can help

reduce the symptoms of IBS. CBT, relaxation therapy, hypnotherapy, dynamic psychotherapy and multicomponent psychological therapy are non-pharmacological methods which are more effective than control therapy.[39] However, none of them is much more effective than the others. It is still uncertain whether this lack of distinction is due to insufficient data, equivalent outcomes or non-specific factors.[40]

PHARMACOLOGICAL METHODS

Antispasmodics are divided into smooth muscle relaxants and antimuscarinics which reduce intestinal motility. They might be an effective treatment for overall symptoms and abdominal pain in IBS. However, in studies, participants taking antispasmodics presented a higher frequency of adverse events such as: visual disturbance, dizziness and dry mouth.[41]

Loperamide functions as an agonist for opioid receptors, resulting in decreased peristalsis and slowed intestinal transit. A randomized controlled trial demonstrated that administering loperamide at bedtime was effective in treating IBS-D. However, combined analyses of these studies revealed no effectiveness in improving overall IBS-D symptoms.[42]

Peppermint oil. Its ingredient, L-menthol, relaxes gastrointestinal smooth muscle by blocking calcium channel receptors. In 10 RCTs (1030 patients) peppermint oil was more effective than a placebo in alleviating abdominal pain and overall IBS symptoms. Unfortunately, the quality of studies was low. Additionally, there is insufficient information regarding which subtype of IBS would derive the greatest benefit. [41,43] Bulking agents and osmotic laxatives can be used to treat patients with IBS-C. Polyethylene glycol, an osmotic laxative, has been demonstrated to be more effective than placebo in improving constipation with good tolerability. However, the same effect was not shown for relieving abdominal pain.[28]

Several studies show improvements in global symptoms of IBS and reductions in pain perception and discomfort, particularly in patients with IBS-D when using tricyclic antidepressants (TCAs). But due to adverse effects such as drowsiness or hypotension, TCAs should be used cautiously. In some studies, on the effectiveness of selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) fluoxetine reduces pain perception, enhances stool consistency and improves bloating symptoms. However, this has not been confirmed in other studies, as well as the effectiveness of citalopram.[44] Antidepressants show better effects in diarrhea-predominant IBS. They could be considered as an alternative therapy for patients suffering from IBS, especially TCAs.[45]

Discussion

Irritable Bowel Syndrome (IBS) is a prevalent gastrointestinal disorder marked by abdominal pain, diarrhea, constipation, and cramps. Diagnosing IBS is challenging due to its varied symptoms and overlap with other conditions. The pathogenesis of IBS involves a complex interplay of psychological, genetic, immunological, and microbiological factors. Psychological distress is notably associated with IBS, significantly affecting patients' quality of life and increasing healthcare utilization. It affects a substantial global population, with prevalence varying by region and gender. Recent evidence highlights roles for immune activation, serotonin dysregulation, bacterial overgrowth, and genetic predisposition. IBS is classified into subtypes based on predominant symptoms. Diagnosis relies on symptom-based criteria, particularly the Rome IV criteria, excluding other diseases through limited testing. Effective management of IBS includes dietary interventions like low FODMAP. Psychological therapies such as CBT and hypnotherapy can alleviate symptoms. Pharmacological treatments, including among others antispasmodics, loperamide, antidepressants vary in efficacy and side effects. IBS is a complex disorder requiring a comprehensive understanding for accurate diagnosis and effective management. Evidence-based treatments can alleviate symptoms and improve quality of life, but ongoing research is essential to refine therapeutic strategies.

Concusions

Irritable Bowel Syndrome (IBS) is a prevalent gastrointestinal disorder widespread in modern community. Psychological distress is closely linked to IBS, significantly impacting patients' quality of life and healthcare utilization. This article summarises all essential pieces of information relating to the aforementioned disease. It was meant to help clinicians with diagnosis and treatment., especially when doctors should primarily base on symptoms. Ongoing research is crucial to further refine therapeutic strategies and improve patient outcomes.

Table 1

	Diagnostic criteria
IBS-C	≥25% of bowel movements of Bristol Stool Form types 1 or 2, and <25% of Bristol Stool Form types 6 or 7
IBS-D	≥25% of bowel movements of Bristol Stool Form types 6 or 7, and <25% of Bristol Stool Form types 1 or 2
IBS-M	≥25% of bowel movements of Bristol Stool Form types 1 or 2, and ≥25% of bowel movements of Bristol Stool Form types 6 or 7
IBS-U	Patients who meet criteria for IBS, but do not fall into one of the other three subgroups according to Bristol Stool Form type

Adapted from[27]

Author's contributions

Kacper Kwiliński: Data curation, visualization

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Karolina Strus: Conceptualization, data curation

Roksana Zdunek: Methodology, investigation

Barbara Wawrzyńska: Methodology, writing - rough preparation

Adrian Kruszewski: Conceptualization, writing - rough preparation, project administration

Natalia Paduszyńska: Conceptualization, supervision

Anna Dąbrowska: Resources, writing - review and editing

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