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Understanding SIBO: A Comprehensive Review of Causes, Symptoms, Diagnosis and Treatment Strategies Of Small Intestinal Bacterial Overgrowth

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ABSTRACT

Introduction

Small intestinal bacterial overgrowth is defined as a pathological condition characterized by excessive proliferation of colonic-type bacteria within the small intestine (>10^5 CFU/mL), accompanied by disturbances in the equilibrium of the small intestinal microbiota. Currently, SIBO is an increasingly prevalent clinical condition, affecting a growing number of patients. The objective of this study is to provide a comprehensive analysis of current research and clinical observations to enhance both diagnostic accuracy and therapeutic strategies for this condition. These advancements are crucial for improving treatment outcomes in patients and broadening the overall understanding of gastrointestinal health.

Materials and Methods

This article presents a comprehensive review of literature derived from the PubMed database, encompassing studies published between 2019 and 2025.

Results

Patients with SIBO typically present with nonspecific gastrointestinal symptoms which complicate the selection of candidates for further diagnostic evaluation. SIBO frequently coexists with other disorders, leading to an underestimation of its actual prevalence. Accurate diagnosis requires a comprehensive assessment, including physical examination and laboratory tests, as well as specialized diagnostic procedures, such as breath tests or small bowel aspiration and culture. Additionally, differential diagnosis is essential to exclude other conditions with similar clinical presentations. The primary treatment strategy involves antibiotic therapy, combined with a low FODMAP diet, aims to alleviate clinical symptoms and improve patients' quality of life by eliminating bacterial overgrowth in the small intestine.

Conclusions

In conclusion, although SIBO is a relatively well-characterized medical condition, further clinical research is still necessary to refine diagnostic methodologies, standardize recognition criteria, and establish specific therapeutic guidelines.

Keywords

"Small Intestinal Bacterial Overgrowth" ; "SIBO diagnosis methods" ; "Breath Test SIBO" ; "Small bowel aspiration" ; "SIBO treatment" ; "low FODMAP diet"

1. Introduction

The gut microbiota encompasses the entirety of microorganisms residing within the human digestive system, including bacteria, viruses, fungi, archaea, and protozoa. The distribution of microorganisms varies across different sections of the digestive system. In the stomach and duodenum, their population is minimal, ranging from 10^3 to 10^4 CFU/mL (colony-forming units per millilitre), due to the acidity of gastric juices and the brief transit time. Conversely, the highest bacterial concentrations are observed in the distal regions of the small intestine and the colon, with approximately 10^8 CFU/mL in the ileum and 10^{11} CFU/mL in the colon. The total number of microorganisms within the human body is estimated to be around 10^{14} CFU/mL, and recent research indicates a roughly equivalent ratio of bacterial to human cells [1].

Small intestinal bacterial overgrowth (SIBO) is defined as a pathological condition characterized by the excessive proliferation of colonic-type bacteria within the small intestine, with concentrations reaching or exceeding 10^5 colony-forming units per milliliter (CFU/mL),

accompanied by a significant disruption of small intestinal microbiota equilibrium [2]. This imbalance, referred to as dysbiosis, disrupts the homeostasis of the small intestinal microbiota, altering the interplay between beneficial commensal bacteria and pathogenic microorganisms within the intestinal ecosystem [3].

This condition results in excessive gas accumulation within the small intestine, accompanied by bloating and umbilical region pain, which may coexist with malabsorption, nutritional deficiencies, and osmotic diarrhea [4]. Neglecting the presence of SIBO may result in metabolic disruptions involving carbohydrates, proteins, fats, and vitamins, alongside alterations in the production of digestive enzymes. Inadequate treatment of SIBO can lead to systemic inflammation and unintended weight loss [5].

This article aims to provide a comprehensive overview of SIBO, including its etiology, clinical manifestations, diagnostic methods, and therapeutic approaches. By synthesizing current research findings and clinical insights, we hope to enhance understanding of this condition and facilitate better management strategies for affected patients. Understanding SIBO is crucial not only for improving individual patient outcomes but also for advancing broader knowledge in the field of gastrointestinal health.

2. Epidemiology

The exact prevalence of SIBO in the general population remains uncertain. Nonetheless, studies indicate its detection ranges from 0% to 20% among healthy control groups [6]. In the physiological state, various mechanisms, including acidic gastric pH, pancreatic enzymes, the intestinal immune system, peristaltic activity, the ileocecal valve, and the intestinal barrier, function to prevent excessive bacterial colonization in the small intestine. Disruption or alteration of any of these protective mechanisms may lead to the development of SIBO [7]. Normal motility in the small intestine may serve as a crucial protective mechanism against the development of SIBO. This motility is regulated by migrating motor complexes (MMCs), which are electrical activity waves that initiate peristaltic movements and facilitate the transit of intestinal contents. Disruptions in these migrating motor complexes lead to stasis of intestinal contents, creating conditions conducive to bacterial colonization and overgrowth [8]. The etiology is therefore multifactorial, involving motility disorders, anatomical abnormalities such as surgical blind loops and obstructions, immune deficiencies, systemic or metabolic conditions, and the long-term use of proton pump inhibitors, resulting in decreased gastric acid secretion and consequently gastric hypochlorhydria [9][10].

The literature has also demonstrated that several conditions, including irritable bowel syndrome, functional dyspepsia, Crohn's disease, chronic pancreatic insufficiency, *H. pylori*

infection, scleroderma, obesity, non-alcoholic fatty liver disease, liver cirrhosis and hepatic encephalopathy are associated with SIBO; however, their precise contribution to the pathogenesis of this disorder remains insufficiently understood. [10][11][12][13].

3. Symptoms

The symptoms of SIBO are typically nonspecific and variable, influenced by the individual patient's condition and the underlying causes of the disorder. Owing to the broad spectrum of symptoms and frequent overlap with other disease entities, accurate data on the prevalence of SIBO remain unavailable [14]. The primary gastrointestinal manifestations include nausea, diarrhea, constipation, flatulence, abdominal distension, and pain. These symptoms may arise from impaired nutrient absorption or alterations in intestinal permeability, coupled with inflammatory responses and immune system activation driven by pathological bacterial fermentation occurring within the small intestine [15]. However, certain patients present without typical intestinal manifestations but instead exhibit weight loss, neuropathy, megaloblastic anemia, peripheral edema, erythema nodosum, or osteomalacia [14]. SIBO often coexists with other gastrointestinal disorders, making it challenging to determine whether it serves as the underlying cause, a resulting consequence, or merely an epiphenomenon of the associated condition [16].

4. Diagnosis

4.1 Fundamental diagnostic methods

Physical examination of patients with small intestinal bacterial overgrowth (SIBO) generally does not reveal significant abnormalities; however, notable abdominal distension may be observed in certain cases. On palpation, segmentally constricted or distended intestinal loops may be detected. In severe cases of SIBO, laboratory findings may reveal abnormalities such as megaloblastic anemia, iron-deficiency anemia, deficiencies in fat-soluble vitamins (A, D, and E), vitamin B12, thiamine, and niacin deficiencies, elevated levels of folate and vitamin K, hypoalbuminemia, and increased fecal fat content [9][17].

4.2 Breath test

Breath testing is widely recognized as the preferred diagnostic method for small intestinal bacterial overgrowth (SIBO), owing to its safety, simplicity, and noninvasive nature. Additionally, this diagnostic approach is broadly accessible and can be conducted at home, providing a convenient solution for patients who are either unable to travel or reside in remote locations [18].

Hydrogen-methane breath testing involves analyzing the components of exhaled gases. This diagnostic method utilizes an orally administered substrate, typically a solution containing a

readily metabolizable carbohydrate, which is subsequently fermented by gut microbiota. Among the most commonly used substrates are glucose and lactulose. Glucose is rapidly absorbed in the proximal small intestine, with minimal amounts reaching the colon, whereas lactulose remains unabsorbed as it transits through the small intestine and directly enters the colon [19]. Upon ingestion of the carbohydrate substrate, microbial interaction leads to the fermentation process, producing gases such as hydrogen, methane, and hydrogen sulfide [20]. Hydrogen and methane gases, generated solely by intestinal bacteria, diffuse through the gut mucosa into the portal circulation, where they are transferred in the alveolar spaces and ultimately exhaled. In healthy individuals, this process primarily begins in the large intestine, which hosts the majority of gut bacteria. Conversely, in patients with SIBO, bacterial fermentation of the substrate takes place proximally within the small intestine. These exhaled gases are collected during normal tidal breathing at regular intervals throughout the breath testing duration [19].

Preparations for the test involve reducing hydrogen and methane gases produced by bacterial fermentation in the colon due to previously ingested food. It is crucial to minimize the influence of medications and lifestyle factors that could alter test outcomes. Diet recommendations include a low-residue diet the day before the test (e.g., white rice, fish, chicken, eggs, white bread, clear broths, plain black tea/coffee), avoiding gum and candy, and an 8-12 hour overnight fast with water only. Medications affecting gut transit time, such as laxatives, prokinetics, opioids, and antibiotics, should be paused prior to testing, depending on tolerability and clinical necessity. European consensus suggests stopping probiotics 24 hours before and delaying breath testing 2 weeks post-colonoscopy. Lifestyle factors such as smoking and exercise must be avoided, as they impact gas production and diffusion rates [19][21].

The breath test is typically conducted in the morning following an 8–12-hour fasting period. After collecting a baseline breath sample, a substrate is administered in a single bolus, and breath samples are collected every 15–20 minutes over a 90–120 minute period to measure hydrogen and methane levels [22].

According to the North American Consensus and Guidelines, the diagnosis of small intestinal bacterial overgrowth is established by observing either an increase in hydrogen levels of at least 20 ppm above baseline, a rise in methane levels of ≥10 ppm above baseline, or a combined elevation in hydrogen and methane levels of ≥15 ppm above baseline within 90 minutes of substrate ingestion [22].

4.3 Small bowel aspiration

Small bowel culture is considered the gold standard for diagnosing SIBO, with a threshold of $\geq 10^3$ CFU/mL recommended for duodenal aspirates and $\geq 10^5$ CFU/mL for jejunal samples.

The procedure involves advancing an endoscope into the duodenum with minimal air insufflation and suction. Subsequently, approximately 3 mL of duodenal fluid is aspirated using a syringe. Once collected, specimens are sent for aerobic and anaerobic cultures to assess bacterial presence effectively. It is crucial to adhere to aseptic techniques during sample collection to prevent contamination. [23].

Small-bowel aspiration and culture are highly accurate in identifying aerobic, anaerobic, and fungal organisms, aiding in the diagnosis of SIBO and assessing colonization severity, considering the duodenum's typically sterile environment. Additionally, microbiological analysis helps in selecting effective antibiotics. However, this method has limitations, such as its invasive nature, high cost, potential sample contamination, challenges in detecting certain bacterial strains, and restriction to diagnosing proximal SIBO [24].

As an alternative to traditional culture-based methods, microbial identification can be conducted using genetic analysis based on 16S ribosomal RNA PCR. However, these techniques are predominantly applied in research and complex differential diagnostics, rather than routine clinical practice for diagnosing SIBO [17].

4.4 Differential diagnostics

In the differential diagnosis of SIBO, conditions causing chronic diarrhea, such as irritable bowel syndrome, celiac disease, and inflammatory bowel diseases, should be considered. In patients without specific risk factors for SIBO, upper and lower gastrointestinal endoscopies are typically performed to exclude alternative conditions, such as atrophic gastritis or Crohn's disease. If endoscopic findings are normal, imaging techniques are employed to identify potential partial obstructions, diverticula, fistulas, or other inflammatory abnormalities. Magnetic resonance enterography, while enhancing diagnostic accuracy for detecting small intestinal strictures, is associated with considerable costs [9].

5. Treatment

The primary objective of SIBO treatment is to eliminate microbial overgrowth in the small intestine to alleviate symptoms. Secondary objectives include sustaining remission, preventing recurrences, and addressing nutritional and vitamin deficiencies. Additionally, SIBO management may encompass dietary interventions, as well as optimizing the treatment

of underlying conditions such as diabetes, cystic fibrosis, or pancreatic insufficiency, and mitigating potential adverse effects of prior surgical procedures [17].

Considering the limitations of current diagnostic methodologies, clinicians frequently employ empiric therapy as a provisional diagnostic approach in cases with a strong suspicion of SIBO. Symptomatic improvement following an antibiotic trial often guides providers toward confirming the diagnosis. Nonetheless, this approach carries inherent risks, including the potential for antibiotic-resistant pathogen development and associated infections, such as Clostridium difficile colitis [6].

5.1 Antibiotics

According to the 2020 North American Consensus, oral antibiotics are a pivotal component in the treatment of SIBO [20]. The majority of studies on SIBO treatment have assessed the effectiveness of amoxicillin clavulanate, ciprofloxacin, doxycycline, metronidazole, neomycin, norfloxacin, tetracycline, co-trimoxazole, and rifaximin [25]. Given the absence of large-scale randomized clinical trials assessing the efficacy of antibiotics in SIBO treatment, antibiotic therapy is predominantly empirical. Furthermore, data comparing the effectiveness of various antibiotics remain scarce. A significant issue associated with antibiotic therapy is the frequent recurrence of the condition and the resulting necessity for repeated treatment. It is important to emphasize that retreatment with antibiotics may increase the risk of antibiotic resistance, diarrhea, including Clostridioides infection, intolerance, and dysbiosis of the gut microbiota [17].

Rifaximin, a nonabsorbable antibiotic, is currently extensively utilized for its broad-spectrum activity against both Gram-positive and Gram-negative aerobic and anaerobic bacteria. By minimizing gastrointestinal absorption while preserving robust antibacterial efficacy, rifaximin has established itself as a potentially effective and safe option for treating SIBO. Its preferred use also arises from a reduced toxicity profile and its proven utility in irritable bowel syndrome, a condition with considerable clinical overlap with SIBO. Notably, rifaximin exhibits "eubotic" properties, preserving colonic flora while increasing the relative abundance of beneficial gut bacteria, such as Lactobacilli and Bifidobacteria. Evidence suggests that the eradication rate of SIBO is dose-dependent, with higher doses yielding greater success [26][6]. Nonetheless, notable limitations persist due to variability across studies and the lack of standardized recommendations regarding optimal dosage and treatment duration [15].

5.2 Diet

FODMAP is an acronym referring to a group of foods, representing fermentable oligosaccharides, disaccharides, monosaccharides, and polyols. FODMAPs are a broad class of small, indigestible carbohydrates containing only 1 to 10 sugar molecules, which are poorly absorbed in the small intestine. They are present in numerous common and diverse food products, such as fruits, vegetables, legumes, cereals, honey, milk and dairy products, as well as sweeteners.

The low-FODMAP strategy extends beyond being merely an "avoidance diet"; it serves as a diagnostic framework for assessing patients' tolerance to specific foods, facilitating their removal from the diet and encouraging substantial lifestyle modifications [27].

The low-FODMAP diet is implemented in three phases, with the ultimate aim of incorporating well-tolerated foods containing limited FODMAPs. Up to 75% of patients typically respond within six weeks or less. Prolonged adherence to the diet beyond four to six weeks is generally discouraged, as it may negatively impact the microbiome and the intake of essential vitamins, minerals, and fiber. Gradual reintroduction of small quantities of FODMAP-containing foods, however, can support the restoration of intestinal microflora by providing crucial prebiotics [28]. This diet is primarily recommended for adults with irritable bowel syndrome (IBS). Given the frequent co-occurrence of SIBO with both IBS and IBD, the 2020 guidelines from the American College of Gastroenterology (ACG) also advocate the use of a low-FODMAP diet for patients with SIBO [29].

5.3 Probiotics and Herbal Substances

Natural therapies involving herbal supplements and pre/probiotics are gaining prominence in the management of SIBO. However, to the best of our knowledge, there are currently no publications that directly compare the use of antibiotics in accordance with established clinical practice guidelines to a combined approach integrating antibiotics, herbal supplements, probiotics, and other natural interventions [30].

5.4 Fecal microbiota transplantation

Fecal microbiota transplantation (FMT) is a therapeutic method involving the transfer of fecal microbiota from healthy donors to patients with microbiome disturbances, aiming to restore gut microbiota balance. Primarily used for refractory *Clostridium difficile* infections, FMT is now being explored as a potential treatment for irritable bowel syndrome, inflammatory bowel disease, and other metabolic disorders. Studies demonstrate a higher prevalence of

small intestinal bacterial overgrowth in IBS patients, suggesting that FMT may positively influence SIBO treatment. Until now, a single documented instance of FMT intervention for SIBO has been recorded, underscoring the imperative for further investigative studies to explain its therapeutic efficacy [31]

Conclusion

Small intestinal bacterial overgrowth (SIBO) is an increasingly common clinical condition affecting patients worldwide. Numerous conditions have been identified as coexisting with SIBO; therefore, it is essential to expand diagnostic evaluation for SIBO in these patients. A broader perspective is necessary for patients presenting with nonspecific gastrointestinal symptoms, along with a thorough diagnostic approach to determine the underlying causes of these complaints. Despite advancements in medical diagnostic techniques, the true prevalence of SIBO remains underestimated. Additionally, diagnostic criteria require standardization to ensure consistency in clinical practice. Currently, there are no clear therapeutic guidelines for SIBO, highlighting the need for further research to evaluate the efficacy of various treatment modalities and their combination.

In summary, SIBO remains a complex and multifaceted clinical condition that requires an interdisciplinary approach to ensure effective patient treatment and improved satisfaction.

Disclosure

Authors do not report any disclosures.

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