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SIBO in pediatric population: literature review on pathogenesis, symptoms, diagnosis and treatment

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Abstract

Introduction:

SIBO is a condition characterized by bacterial overgrowth in the small intestine which is caused by various factors. The excessively proliferated bacteria can lead to digestive disturbances- manifesting as gastrointestinal symptoms and malabsorption. In pediatric patients, small intestinal bacterial overgrowth can also result in growth retardation. Due to many challenges related to the diagnosis and treatment of children- this condition should be well known by pediatric healthcare providers.

Aim of the study:

This study aims to summarizes the recent knowledge about the pathogenesis, symptoms, diagnosis and the treatment of small intestine bacterial overgrowth in pediatric population, providing an overview for healthcare professionals.

Material and methods:

The literature available in the PubMed database was reviewed using the following keywords: „SIBO", „Small Intestinal Bacterial Overgrowth", ,, „SIBO in pediatric population", „Endoscopy in children", „SIBO treatment"

Conclusion:

Small intestinal bacterial overgrowth is a complex disorder that can have a significant influence on the quality of life of pediatric patients. The variety of symptoms of this syndrome can lead to confusing clinical findings. The diagnostic pathway consists of a clinical evaluation and specific tests, to verify the presence of bacterial overgrowth. Effective treatment involves modifying the intestinal microbiota - mostly through antibiotic therapy - and supplementing nutritional deficiencies. Probiotics and dietary modifications, such as low-FODMAP diets, are often used as adjunctive therapies.

Keywords: „SIBO", „Small Intestinal Bacterial Overgrowth", „SIBO in pediatric population", „gastrointestinal symptoms", „SIBO diagnosis"

Introduction

Small intestinal bacterial overgrowth (SIBO) is characterized by an abnormal increase in the number of bacteria in the small intestine. This condition leads to various gastrointestinal symptoms including bloating, diarrhea, and malabsorption. The normal small intestine contains relatively few bacteria compared to the colon, due to various protective mechanisms such as gastric acidity, intestinal motility, and the immune response of the mucosa. Disruptions in these protective mechanisms can lead to bacterial overgrowth. [1] While SIBO is well-documented in adult populations, its prevalence and impact on pediatric patients are less understood. Children, particularly those with chronic diseases such as cystic fibrosis, celiac disease, and irritable bowel syndrome (IBS), appear to be at increased risk for developing SIBO. [2] Chronic conditions can disrupt the normal motility and immune functions of the gastrointestinal tract, creating an environment conducive to bacterial overgrowth. [3]

Pathogenesis and predisposing factors

The disruption of multiple protective mechanisms that occurs can lead to bacterial overgrowth, which is often seen in conditions such as irritable bowel syndrome, immune deficiencies and post-surgical conditions. [4] One of the primary inhibitors of bacterial growth in the small intestine is gastric acid. Disruption of its secretion and consequently reduced amount or using of proton pump inhibitors (PPIs) can abolish this protective effect, resulting in an increased risk of SIBO. [5] Another key factor in preventing bacterial overgrowth in the small intestine is peristalsis. Effective movement of intestinal content prevents stasis and helps protect against excessive microbial proliferation. [6] Therefore, conditions such as irritable bowel syndrome (IBS) can dysregulate normal intestinal motility, fostering an environment conducive to bacterial overgrowth. [7] One of the factors that can also affect small bowel motility disorders is obesity. Furthermore, it promotes the appearance of bacterial overgrowth in a range of other ways, including a different composition of the microbiota, and increased permeability of the small intestinal wall compared to normal-weight patients. [8] It should also be remembered that surgical procedures in the abdomen, especially those involving the gastrointestinal tract, can disrupt the normal anatomy and intestinal motility, increasing the risk of bacterial proliferation. [3] The immune system, particularly the mucosal immune response,

helps in controlling bacterial populations in the gut. [1] When there are congenital or acquired immunodeficiencies, the immune response weakens, allowing bacterial overgrowth to occur. As a result, SIBO has been associated with hypogammaglobulinemia, as well as with disorders affecting cellular immunity. [6]

Symptoms

The clinical manifestation of SIBO in children is varied and includes gastrointestinal, systemic or neurological symptoms. Bacterial overgrowth in the small intestine can also lead to mood and growth disorders. Many of these symptoms are non-specific and occur in other gastrointestinal diseases, triggering diagnostic challenges. Additionally, these symptoms can be mistakenly attributed to the underlying disease that causes SIBO. [9]

Gastrointestinal symptoms

Diarrhea- chronic or recurrent; is a common symptom, often caused by nutrient malabsorption due to bacterial disruption of digestive processes. [10] This can lead to frequent, loose, and watery stools, which can be particularly distressing for children and their caregivers. [11]

Constipations- has been observed in methanogenic SIBO- where specific enteric bacteria generate methane during fermentation [9]

Abdominal pain- children with SIBO frequently experience abdominal pain or cramping, which can be diffuse or localized, often exacerbated by eating. [1] The pain is usually described as a dull, aching sensation, and can be intense enough to interfere with daily activities. [12]

Bloating- is often accompanied by a visible expansion of abdominal circumference, and fluctuate during the day; it can be caused by the fermentation process which takes place in the small intestine. [13]

Flatulence- increased gas production can lead to recurrent flatulence, which can be distressing and socially uncomfortable for children. [1] The gas often has an unpleasant scent because bacteria ferment undigested food in the guts. [14]

Nausea- this symptom can cause reduced appetite and an aversion to food. [15]

Malabsorption- bacterial overgrowth can interfere with the digestion and absorption of nutrients. [10] It manifests itself in symptoms such as weight loss and insufficiencies in for example fat-soluble vitamins, iron and folic acid in erythrocytes. [16]

Systemic Symptoms

Vitamin Deficiencies- SIBO can cause deficiencies in fat-soluble vitamins and vitamin B12 as a result of impaired absorption and usage of these nutrients by bacteria. [13] These deficiencies can manifest such as night blindness due to lack of vitamin A, rickets caused by an insufficient amount of vitamin D, easy bruising due to vitamin K deficiency and neurological problems resulting from vitamin B12 deficit. [17]

Weight Loss- malabsorption and chronic diarrhea can result in a significant weight loss and impaired growth in children. [12]

Fatigue- chronic malabsorption and nutritional deficiencies can result in fatigue and reduced physical endurance. [10] For example vitamin D and vitamin B12 deficiencies can reduce energy levels and general well-being, causing chronic fatigue. [18]

Anemia- resulting from impaired absorption and consumption of nutrients by bacteria which leads to vitamin B12 deficiency. [15] Anemia can cause shortness of breath and dizziness, further impacting the child's quality of life. [14]

Delayed growth and developmental delays- result from malabsorption and deficiencies; the potential occurrence of protein malabsorption also contributes to growth disorders. [19] Severe nutritional deficiencies can also lead to developmental delays, affecting both motor and cognitive development. [17]

Irritability and mood swings- nutritional deficiencies and ongoing discomfort from gastrointestinal symptoms can lead to irritability and mood swings in children. These conditions impacting their overall well-being and can cause behavioral changes, affecting their daily interactions and quality of life. [12]

Cognitive impairment and peripheral neuropathy- chronic vitamin B12 deficiency can lead to cognitive impairments, including memory loss and difficulty concentrating. [13] It can also manifest as a neurological symptoms including hand shaking, tingling, paresthesias and unclear vision. [20] This can lead to difficulties with coordination and balance. [11]

Diagnosis

Diagnosing SIBO in pediatric population includes a combination of clinical evaluation and diagnostic tests. Clinical history and physical examination are crucial for identifying possible cases of SIBO. Physicians should look for symptoms of malabsorption, chronic diarrhea and stomach pain. A comprehensive nutritional interview can also provide guidance, as symptoms often correlate with specific foods. [14]

Small intestinal bacterial overgrowth can be detected by both invasive and non-invasive techniques. Non-invasive methods primarily include breath tests that can detect bacteria-produced gases. Invasive methods include culture-dependent techniques, such as obtaining and culturing samples of small bowel liquid, and culture-independent approaches, such as DNA sequencing to determine the population of bacteria. [9]

The breath test is cost-effective, non-invasive and relatively easy to perform. It has many limitations and is one of the less precise methods; however, its simplicity of use and accessibility have made it one of the most widely used diagnostic tools for SIBO. [15] This test is particularly useful in the pediatric population, where the low invasiveness of testing plays a crucial role. [9] [21] After ingesting a carbohydrate substrate (usually lactulose or glucose), breath samples are collected at regular intervals to measure hydrogen levels. Elevated hydrogen levels indicate bacterial fermentation in the small intestine. [14] Research shows that for diagnosing SIBO, using glucose rather than lactose for testing remains a better choice. [22] One of the major problems with performing this test is that it is not possible to determine the exact location within the intestine where the given substrate is metabolized. [23] In addition to hydrogen, methane levels can also be measured. SIBO that runs with the production of a large amount of methane is characterized by the occurrence of constipation in patients. The production of methane is attributed to the presence of some bacteria that generate it, like for example Methanobrevibacter smithii. [13]Methane detection indicates a different type of bacterial overgrowth, which can affect treatment decisions. [24] However, many authors support the fact that the hydrogen test is more appropriate for use than the methane test. [25] It is also relevant that the hydrogen or methane breath test generally has no serious adverse effects. The only recorded ones are occasional stomach pains or emesis occurring while undergoing the procedure. [9]

One of the invasive methods to diagnose SIBO is the sampling of the material for analysis during an endoscopy. Material from the small intestine is taken during gastrointestinal endoscopy with a sterile catheter. Subsequently, the collected aspirate is cultured to detect either aerobic or anaerobic bacteria. It is relevant that nowadays this method is considered as the gold standard. These procedures are not only invasive but also costly and can only be performed by adequately trained physicians. These components greatly limit their ability to be used in some circumstances. [9] In addition, for children, performing this procedure often requires anesthesia and exposes them to potentially traumatizing experiences. [26] For these reasons, this invasive procedure is usually used as only in complicated cases or when other diagnostic approaches are inconclusive. [27] Available modern methods for detecting bacterial overgrowth in the small intestine include next-generation sequencing. Despite the widespread use of this type of diagnostics in many fields of medicine, in the case of SIBO these methods are still under-described and currently have little clinical application. [9]

One of the pathogenetic elements of SIBO that we can detect in additional tests is the existence of increased intestinal permeability. Information about the presence of leakage in the small intestine can be provided by tests that measure the absorption of lactulose and mannitol. [14]

There are other diagnostic possibilities that can direct us to the diagnosis of SIBO. Some of the laboratory tests can give results to determine the presence of disturbances occurring in the course of bacterial overgrowth. Evaluation of vitamin levels, especially vitamin B12, can uncover malabsorption associated with SIBO. Deficiencies in fat-soluble vitamins (A, D, E, K) and other nutrients can also signalize bacterial overgrowth. [14] Laboratory tests can additionally reveal anemia along with lymphopenia. It is also possible to detect abnormalities indirectly indicative of malnutrition- reduced levels of prealbumin and transferrin. [25] These findings are nonspecific, but can be helpful in establishing a diagnosis when are used in conjunction with other findings.

Stool examinations showing a significant fat content(steatorrhea) may also suggest a diagnosis of SIBO, of course, after excluding other diseases from the differential diagnosis. Diagnostic opportunities will also be found when imaging studies are used. CT eneterography can visualize the cause of intestinal stasis, which may lie at the root of SIBO. [28]

Diagnostic challenges

Although many diagnostic methods are available, the diagnosis of bacterial overgrowth of the small intestine can still cause numerous difficulties. First of all, the clinical assessment often remains confusing. Symptoms appearing in the course of SIBO are uncharacteristic and may be indicative of many disease states in gastroenterology and beyond. [13] In addition, bacterial proliferation in the small intestine often coexists with other diseases like IBS, celiac disease and cystic fibrosis. Symptoms of the underlying disorders can also cover up the existence of SIBO. Distinguishing bacterial overgrowth from these conditions demands careful clinical assessment and adequate usage of diagnostic tests. [14]

Treatment

Treatment of SIBO in children includes both pharmacological and non-pharmacological management. It should be based on key areas that include modifying the enteric microbiota, supplementing nutritional insufficiencies, treating the disorders that lead to SIBO, and preventing the reoccurrence of the condition. [10]

Pharmacological treatments

Antibiotics

Obtaining samples for culture is a diagnostic challenge for this reason, identification of the SIBO-causing microorganisms in the heterogeneous small intestinal ecosystem is rarely achievable. Due to this, the most common type of therapy is empirical antibiotic treatment. [9]

Available studies indicate that antibiotics are an effective treatment for SIBO in children, and despite the availability of other antibiotics (such as metronidzaol, ciprofloxacin) rifaximin appears to be the most effective. In addition, the safety of using rifaximin has been proven on the largest number of patients and studies. [9] The most common treatment regimen for rifaximin is to use it for 7 to 10 days, depending on the clinical presentation. When treating SIBO, it is beneficial to use higher than standard doses. Rifaximin, in addition to eliminating the discomfort associated with bacterial overgrowth, also reduces the amount of bacteria presence up to 80%. [29] However, it should be remembered that in the case of SIBO occurring with the dominance of methane-producing bacteria in the intestine, antibiotic therapy can be more complicated due to multi-antibiotic resistance of these bacteria. [15]

Probiotics

Probiotics can be used as adjunctive therapy to help re-establish a healthy intestinal microbiota. Strains such as Lactobacillus and Bifidobacterium have shown promise in reducing SIBO symptoms by enhancing the intestinal barrier function, inhibiting the growth of pathogenic bacteria, and modulating the immune response, which collectively contribute to the alleviation of SIBO symptoms and the restoration of gut health. [10] However, there are studies that show that taking probiotics by patients with SIBO leads to adverse effects like bloating, metabolic lactate acidosis and cognitive impairment. These manifestations were resolved upon discontinuation of probiotics and introduction of antibiotic treatment. Given the current lack of proven relevance in the use of probiotics in patients with SIBO, further clinical trials are needed to conclusively determine their effects. For this reason, the inclusion of probiotics in patients with bacterial overgrowth should be carefully evaluated on an individual basis. While probiotics can offer benefits, they also have the potential to worsen the patient's condition and exacerbate symptoms. [30]

Non-Pharmacological Treatments

A low FODMAP diet that decreases fermentable oligosaccharides, disaccharides and monosaccharides. By limiting foods that are poorly absorbed and fermentable, a low FODMAP diet reduces the amount of substrates that are available for bacterial fermentation, thus reducing bloating and other gastrointestinal symptoms associated with SIBO. [31] The diet involves limiting foods high in FODMAP, such as certain fruits (apples, pears), vegetables (onions, garlic), dairy products and wheat-based products. Patients usually follow a strict low-FODMAP phase for few (4-6) weeks, followed by a re-introduction phase to identify specific triggers. [32] However, it should be remembered that the low-FODMAP diet is eliminatory and highly restrictive. For patients at risk of developing malnutrition, which can occur in SIBO, this type of diet can be a kind of risk. [9]

There are also indications of the benefits of restricting the dietary intake of malabsorbable fats in the early stages of treatment. Their consumption in larger quantities can promote bacterial growth in the small intestine and cause bloating. [10]

Addressing nutritional deficiencies is a crucial aspect of managing SIBO, particularly in pediatric patients who are at risk of growth and developmental delays. Because of the impaired absorption and risk of malnutrition, especially fat-soluble vitamin deficiencies associated with SIBO, supplementation of these nutrients is crucial. Dietary management should be an integral part of the therapy of patients with small intestinal bacterial overgrowth.

[13] Working with a dietician to develop a well-balanced diet suited to children's nutritional needs while treating SIBO symptoms can be highly beneficial. This approach ensures that the nutrition plan targets specific nutritional deficiencies and identifies food triggers that aggravate symptoms, resulting in supporting the child's overall health and development. [33]

Physical activity and normal weight of the child are also basic to maintain proper bacterial flora within the gastrointestinal tract. [34]

SIBO is characterized by the possible appearance of recurrence, which sometimes requires repeated courses of antibiotics or other therapies. [12] Regular follow-up is key to monitoring for recurrence of SIBO and implementing appropriate therapy as needed. Periodic reassessment with targeted tests (for example breathing tests) or clinical evaluation can support early recognition of recurrences. [14]

Conclusions

Small intestinal bacterial overgrowth in pediatric patients is a multifaceted condition that can significantly affect growth and overall health due to impaired nutrient absorption. Although it is a benign syndrome nevertheless the recurrent and chronic gastrointestinal symptoms lead to significant discomfort for the child, which can impair normal psychosocial development.

The wide spectrum of non-specific manifestations can lead to diagnostic challenges and delays in correct diagnosis. Available diagnostic methods remain imperfect and require a comprehensive approach to the patient. Frequent co-occurrence of SIBO with other diseases makes the diagnosis of bacterial overgrowth frequently neglected. One of the most widely used diagnostic methods- hydrogen breath test- despite being an defective method is relatively simple to perform on cooperating pediatric patients. Treatment which consist of antibiotic therapy and promotion of proper small intestinal bacterial flora based on probiotics appears to be very effective. Great importance is placed on dietary management for SIBO, particularly by reducing the intake of malabsorbed fats and implementing a low FODMAP diet. These dietary modifications can help alleviate symptoms and accelerate recovery.

Early diagnosis and effective treatment are essential to improve clinical results and potentially prevent developmental disorders. Ongoing research and customized therapeutic approaches are fundamental to improving outcomes for affected children.

Author's contribution

Conceptualization, Martyna Opatowska; methodology, Martyna Opatowska and Joanna Jakubiec; software, Julita Gmitrzuk and Anna Jachymek; check, Joanna Jakubiec and Marta Piotrowska; formal analysis, Martyna Opatowska and Zuzanna Malinka; investigation, Martyna Opatowska and Tomasz Kucharski; resources, Joanna Jakubiec and Anna Jachymek; data curation, Julita Gmitrzuk and Marta Piotrowska; writing – rough preparation, Martyna Opatowska; writing - review and editing, Martyna Opatowska and Marta Piotrowska; visualization, Martyna Opatowska, Zuzanna Malinka and Tomasz Kucharski; supervision, Katarzyna Wiśniewska and Julita Gmitrzuk; project administration, Martyna Opatowska, Katarzyna Wiśniewska. All authors have read and agreed with the published version of the manuscript.

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