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SIBO – what the general practitioner should know

SIBO – co lekarz rodzinny wiedzieć powinien

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Abstract

Healthy gut microbiota performs many important functions and is necessary for maintaining the body in a state of metabolic equilibrium. Unfavourable conditions may lead to the development of small intestinal bacterial overgrowth (SIBO), a condition defined as an excessive bacterial colonisation of the small intestine. The prevalence of SIBO in the general population is still unknown. Some risk factors which have been implicated in the pathogenesis of SIBO include disorders of gastrointestinal motility, history of intestinal resection, chronic comorbidities, and elderly age. SIBO may present with a range of non-specific symptoms, the most common of which are bloating and abdominal distension, nausea, abdominal pain, bowel movement disorders, lack of appetite or unintentional weight loss. SIBO is diagnosed by invasive tests and the increasingly popular non-invasive breath tests. Supplementary diagnostic examinations include microscopic evaluation of stool for the presence of fat, complete blood count, and measurement of vitamin B12 or albumin levels. First-line treatment is based on eubiotics, one of which is rifaximin-α. The drug is characterised by a broad spectrum of activity against a variety of Gram-negative and Gram-positive bacteria, both aerobic and anaerobic. A major component of SIBO therapy is appropriate diet combined with lifestyle modifications (regular physical activity, avoidance of stress, and restoration of normal sleep pattern). In rare cases, for example in patients with anatomical anomalies, surgical management should be considered. The paper presents basic information about SIBO, which is useful in the everyday practice of primary care physicians.

Keywords: SIBO, bacterial overgrowth, gut microbiota, rifaximin-α

Streszczenie

Prawidłowa mikrobiota jelitowa pełni wiele istotnych funkcji i jest niezbędna do utrzymania równowagi metabolicznej organizmu. W niesprzyjających warunkach może dojść do rozrostu bakteryjnego jelita cienkiego (SIBO), definiowanego jako kolonizacja jelita cienkiego przez mikrobiotę typową dla jelita grubego. Odsetek występowania SIBO w populacji ogólnej jest wciąż nieznany. Do czynników predysponujących do wystąpienia rozrostu bakteryjnego zalicza się między innymi zaburzenia motoryki przewodu pokarmowego, stan po zabiegach resekcyjnych w obrębie jelit, współistnienie chorób przewlekłych czy starszy wiek. Zespół ten charakteryzuje się występowaniem niespecyficznych objawów, do których najczęściej można zaliczyć wzdęcia, nudności, bóle brzucha, zaburzenia wypróżniania, brak apetytu czy spadek masy ciała. SIBO rozpoznaje się na podstawie testów inwazyjnych i coraz bardziej popularnych nieinwazyjnych testów oddechowych. Pomocniczymi badaniami są również ocena mikroskopowa kału na obecność tłuszczu, oznaczenie morfologii, stężenia witaminy B12 czy albumin. Leczenie pierwszego rzutu stanowią eubiotyki, których przykładem jest ryfaksymina α, charakteryzująca się szerokim spektrum działania – wpływa na bakterie Gram-ujemne i Gram-dodatnie, zarówno tlenowe, jak i beztlenowe. W terapii SIBO istotne są również odpowiednia dieta i modyfikacja stylu życia (regularna aktywność fizyczna, unikanie stresu oraz przywrócenie rytmu snu). W rzadkich przypadkach, jak np. zmiany anatomiczne, wskazane jest rozważenie leczenia operacyjnego. Niniejsza praca zawiera podstawowe informacje dotyczące SIBO, przydatne w codziennej praktyce lekarza podstawowej opieki zdrowotnej.

Słowa kluczowe: SIBO, rozrost bakteryjny, mikrobiota jelitowa, ryfaksymina α

INTRODUCTION

Small intestinal bacterial overgrowth (SIBO) is a clinical syndrome presenting as the proliferation of bacterial populations in the small intestine over 10^6 CFU (colony-forming units) per millilitre of intestinal fluid. The bacterial count found in normally colonised gastrointestinal (GI) tract varies considerably. It is the lowest in the upper GI tract (10^3 CFU/mL in duodenum), but in the ileum the count increases to 10^8 CFU/mL, and in the large intestine it reaches 10^{11}–10^{14} CFU/mL[1]. Gastrointestinal microbiota plays an important role in maintaining the body's homeostasis. Among other functions, it is involved in metabolic processes (bacterial fermentation, vitamin metabolism), and protects the intestinal epithelium. In addition, it contributes to the proper functioning of the immune system. Disorders in the quantitative and qualitative composition of gut microbiota are known to contribute to the development of SIBO.

A number of risk factors predisposing to SIBO have been identified. One of them is poor gut motility, which causes the intestinal content to stay longer in the gut, and ultimately leads to increased fermentation processes and bacterial proliferation. These disorders are quite common, for example, in patients with long-term diabetes mellitus. The prevalence of SIBO among diabetics has been shown to be higher[2], which is attributed to visceral neuropathy, among other factors[3]. Other groups in which SIBO is thought to be more prevalent compared to the general population include patients with hypothyroidism[4], systemic sclerosis[5], and in some patients with irritable bowel syndrome (IBS)[6]. These conditions are associated with migrating myoelectric complex causing disruption of intestinal motility.

Another risk group consists of patients with congenital anatomical anomalies (intestinal duplication, diverticula) or acquired alterations in the intestines (for example resulting from ileocecal resection, e.g. secondary to Crohn's disease, or bypassing anastomoses). The disorders enumerated above carry the risk of retrograde colonisation of the small intestine[7]. In patients after ileocecal resection, the lack of anatomical barrier (Bauhin's valve) causes the reflux of colonic contents into the small intestine.

Also, an increased predisposition to the development of SIBO has been found in patients with chronic pancreatitis (ChP). Based on the results of hydrogen breath test, Trespi and Ferrieri diagnosed SIBO in 34% of patients with ChP[8]. The observation may be attributed to a disturbance of the exocrine pancreatic function (elimination of the antibacterial effect of proteolytic enzymes), and frequent alcohol consumption and smoking noted in this group of patients.

Excessive fructose consumption often observed among patients with non-alcoholic fatty liver disease leads to an intense fermentation process resulting in bacterial overgrowth. Studies have also shown that portal hypertension in patients with cirrhosis increases the risk of SIBO[9]. Furthermore, the prevalence of SIBO is higher in the population with an impairment of the immune system including acquired immunodeficiency syndrome (AIDS), immunoglobulin A (IgA) deficiency, and cachexia[10].

The prevalence of SIBO in the general population is unknown. The disorder is more frequently diagnosed in the elderly[11], which is most likely related to a more widespread prevalence of disorders of gastrointestinal motility, achlorhydria due to atrophic gastritis, and the use of proton pump inhibitors in this age group[12].

SYMPTOMS

SIBO presents with a range of non-specific symptoms which are similar to those occurring in many other gastrointestinal disorders such as lactose intolerance (affecting approximately 20–25% of the adult Polish population[13]), other food intolerances, IBS, and even cancer. The most common clinical manifestations of SIBO include bloating and abdominal distension, nausea, abdominal pain, bowel movement disorders (diarrhoea, constipation), and unintentional weight loss. Over time, other manifestations may develop: vitamin deficiencies (vitamin B_{12} – neuropathies, burning tongue sensation; vitamin D – disorders of bone metabolism; vitamin A – nyctalopia, skin lesions)[14].

DIAGNOSTIC WORK-UP

The diagnostic work-up for SIBO generally involves hydrogen- and hydrogen and methane-based breath testing. The method is both simple and non-invasive. Substrates include readily metabolised carbohydrates such as lactulose, glucose, sucrose or xylose. The breath test measures the concentration of hydrogen in exhaled air. Hydrogen is formed in the process of fermentation of the above-mentioned substrates by small intestinal bacteria. The diagnostic sensitivity and specificity of breath tests are estimated at 62.5% and 77.8%, respectively[15]. The disadvantages of hydrogen breath testing include standardisation issues, and the potential effect of antibiotics, salicylates or smoking on the results[16]. In addition, non-hydrogen-producing microbiota is known to be present in up to 27% of patients. The duration of testing ranges from 1 to 3 hours. Absolute contraindications to breath tests include hereditary fructose intolerance and suspected reactive hypoglycaemia. The method of direct quantitative evaluation of bacterial populations in the small intestinal aspirate tends to be less commonly used nowadays, as it is technically difficult, expensive, and time-consuming. In addition, there is a risk of sample contamination by bacteria residing in the stomach or oral cavity. Despite these disadvantages, the method

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is still recognised by some as the gold standard in the diagnosis of SIBO. Bacterial cultures usually show the growth of *Lactobacillus*, *Escherichia coli*, *Streptococcus* or *Bacteroides*.

A supplementary diagnostic tool is microscopic faecal fat test (e.g. Sudan stain), as SIBO patients have an increased number of fat globules in the stool.

The diagnostic work-up for SIBO should also include complete blood count and measurement of vitamin B_{12} and albumin levels, as the disorder is known to be linked to megaloblastic anaemia and hypoalbuminaemia.

TREATMENT

SIBO treatment includes pharmacotherapy, dietary interventions, and in some cases also surgical management. A major component of treatment is lifestyle changes. Regular physical activity, avoidance of stress, and restoration of normal sleep pattern are recommended.

One of the most widely used pharmacotherapeutic agents is rifaximin-α. The eubiotic has a broad spectrum of activity against Gram-negative and Gram-positive bacteria, both aerobic and anaerobic. An additional advantage of rifaximin-α is that it is not associated with the development of resistance. Rifaximin-α indirectly reduces the inflammatory response of intestinal cells by inhibiting the activation of the nuclear factor kappa B (NF-κB), and down-regulating proinflammatory cytokines. In addition, it mediates interbacterial communication, reducing the adhesion, aggregation, translocation and virulence of bacteria.

Rifaximin-α is virtually not absorbed from the gastrointestinal tract (<1%). It is pharmacologically active only in the intestine, where it exerts a stabilising effect on the gut microbiota. As a result, systemic adverse effects during treatment are relatively rare. A 2017 meta-analysis demonstrated the efficacy of rifaximin-α in SIBO therapy in over 67% of patients, with a low percentage of adverse effects[17]. Available studies show that an effective therapeutic regimen is based on the dose of 1,200–1,650 mg/day for 10–14 days[18,19]. Such treatment cycles can be used for several months. Also, recent studies have revealed a potential for enhancing the efficacy of rifaximin by supplementing the treatment with soluble fibre preparations or probiotics[20–23].

Antibiotics are no longer recommended in the therapy of SIBO because of the risk of adverse reactions[24]. Previously used therapeutic modalities included metronidazole, tetracyclines, amoxicillin with clavulanic acid, and fluoroquinolones.

Another important drug group, indicated especially in patients with long-term diabetes or hypothyroidism and suspected gastroparesis, are prokinetics[25]. An example is cisapride – a serotonin 5-HT_4 receptor agonist. The drug should be used at a dose of 10 mg 3–4 times a day, about 15 minutes before meals and at bedtime. Aside from gastroparesis, the drug is not intended for long-term use, as treatment is associated with the risk of adverse reactions which often include abdominal pain and diarrhoea, and occasionally gynaecomastia. Severe anaphylactic reactions are more uncommon. From the clinical point of view, however, the most important is the risk of cardiac arrhythmias. Consequently, the drug is contraindicated in patients with heart conditions. Another prokinetic drug is itopride, which works by blocking D_2-class dopamine receptors, and inhibiting acetylcholinesterase activity. It is usually taken at a dose of 50 mg, 3 times a day before meals.

An important component of SIBO therapy is dietary treatment. The intake of medium chain fatty acids is indicated. There have been reports claiming that symptoms of SIBO can be reduced by using the low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet, i.e. a dietary regime consisting in the restriction of fermentable oligo-, di- and monosaccharides, and polyols. This diet has produced benefits in many IBS patients[26]. The risk of SIBO in this group is approximately five times higher than in the control group[27], and the disorders are often found to coexist. The use of the above diet in SIBO seems justified because it is common for patients with SIBO to have carbohydrate intolerance[28].

Patients with chronic diarrhoea and malabsorptive disorders may develop vitamin and mineral deficiencies. In such cases, appropriate supplementation is indicated.

The effect of probiotics on the course and treatment of SIBO is unclear and requires more research[29]. Some authors have found probiotics to be effective[30,31], while others have not demonstrated any benefits of probiotic supplementation[32]. In diabetic patients, probiotics have been shown to have a positive effect on controlling glucose levels[33] and reducing insulin resistance[34,35], and exert a protective action on pancreatic beta cells[36]. In cases involving anatomical anomalies in the intestines (intestinal stenosis, interloop fistulas), surgical treatment should be considered.

CONCLUSIONS

Small intestinal bacterial overgrowth is characterised by a range of symptoms which are encountered by primary care physicians in their daily practice. SIBO should be included in the differential diagnostic work-up, especially in high-risk patients (elderly individuals, with a history of intestinal resection, affected by chronic conditions). Owing to the availability of non-invasive diagnostic methods and highly effective therapies, the quality of life of patients diagnosed with SIBO can be improved within a short time.

Conflict of interest

The authors do not declare any financial or personal links with other persons or organisations that might adversely affect the content of the publication or claim any right to the publication.

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