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POSSIBLE CAUSES OF CHANGES IN THE INTESTINAL MICROBIOME

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Abstract
Irritable bowel syndrome (IBS) is one of the most common gastrointestinal tract (GIT) diseases. The prevalence of IBS in Europe and North America is approximately 9.8%-12.8%. At the same time, 27-82.6% of patients with IBS have symptoms of functional dyspepsia (FD). The disease significantly worsens the quality of life, reduces the social activity of patients, and requires significant material costs for their examination and treatment. If the diagnosis of IBS is established only on the basis of patient complaints, the absence of alarm symptoms and a minimum number of laboratory and instrumental studies, as recommended in the Rome III criteria, the probability of making an incorrect diagnosis remains quite high (up to 25%). The effectiveness of most recommended drugs and regimens in the treatment of IBS does not exceed 38%, which indicates insufficient study of the pathogenesis of the disease. Approaches to the treatment of combined functional gastrointestinal disorders (for example, IBS and functional dyspepsia syndrome) have not been developed. In recent years, studies have shown that in addition to the emotional component, structural changes contribute to the development of IBS symptoms. The following are discussed: increased intestinal wall permeability due to impaired synthesis of proteins that form tight junctions between epithelial cells ; changes in the expression of signaling receptors that mediate the interaction of the host organism with bacterial cells; abnormal cytokine profiles with increased levels of proinflammatory cytokines; the presence of nonspecific inflammation in the intestinal wall; and changes in the qualitative and quantitative composition of the intestinal microflora. However, the relationship between the above changes and the development of disease symptoms remains poorly understood. It seems relevant to conduct a more in-depth study of the structure of functional diseases; assess the feasibility of performing a set of laboratory and instrumental examinations to establish a diagnosis; and determine optimal treatment regimens for such patients depending on the effect of drugs on the underlying mechanisms of symptom development.

INTRODUCTION

The aim of the study to study the clinical and pathophysiological characteristics of functional gastrointestinal diseases in patients in the Republic of Uzbekistan.

OBJECTIVES AND METHODS OF THE STUDY

To assess the frequency of detection and structure of diagnoses of functional gastrointestinal diseases in a multidisciplinary hospital. To determine the frequency of erroneous diagnoses of patients with functional gastrointestinal diseases in outpatient practice. To assess the feasibility of

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webofjournals.com/index.php/5

using in clinical practice a Questionnaire reflecting the presence, intensity and dynamics of symptoms of functional gastrointestinal diseases against the background of the treatment.

RESULTS OF THE STUDY

Irritable bowel syndrome (IBS) is one of the most common gastrointestinal diseases, the main manifestations of which are abdominal pain, flatulence, and changes in stool consistency and frequency. According to various authors, the prevalence of IBS in the world ranges from 4 to 30%. The disease significantly worsens the quality of life of patients and requires significant material costs for the treatment and examination of patients. Despite the fact that the history of the study of functional disorders has been going on for more than 100 years, many questions regarding the etiology, pathogenesis, and treatment tactics still have no clear answer. Initially, the cause of symptoms in IBS was considered to be motor and sensitivity disorders that occur in the absence of structural, organic, or known biochemical pathology, in genetically predisposed individuals under the influence of unfavorable environmental factors against the background of psychoemotional stress or a previous intestinal infection. However, already at the end of the last century, this point of view was criticized. Thus, D.S. In 2018, D.S. Sarkisov wrote that the diagnosis of "irritable bowel syndrome" is not purely functional, but has its own structural equivalent, a morphological basis. Current state of the problem. From today's perspective, ideas about the pathogenesis of IBS have undergone significant changes. Much attention is paid to possible changes in the structure and function of the enteric nervous system. The enteric nervous system, which coordinates motility and secretion of the gastrointestinal tract, contains more than 100 million nerve cells grouped into the myenteric plexus of Auerbach and submucous plexuses. Neurons of the myenteric plexus mainly regulate motility, and neurons of the submucous plexus are involved in maintaining homeostasis. Almost all known mediators are represented in the enteric nervous system. Such a complexly organized system can ensure the functioning of the gastrointestinal tract independently, reacting to the slightest changes in the intestinal microflora, cytokine profile, etc. However, to ensure optimal functioning of the gastrointestinal tract, the regulatory influence of the central nervous system is necessary. In patients suffering from IBS, changes are determined that can lead to disruption of the functions of the enteric nervous system: disruption of the qualitative and quantitative composition of the intestinal microflora, inflammatory changes in the intestinal wall, which leads to a change in the state of the receptor apparatus of the pain sensitivity pathways. The identified changes are interconnected with each other and form a logical chain, the completion of which is the development of disease symptoms. However, it remains unclear whether the above-described disorders determine their severity and nature, since the influence of structural and morphological elements in patients with functional diseases is often superimposed by psychological and mental components, which often overlap the primary organ symptoms. In recent years, the problem of qualitative and quantitative changes in the composition of intestinal microflora in patients suffering from IBS has been widely discussed. For example, bacterial overgrowth syndrome (SIBO) occurs in such patients 6 times more often than in healthy individuals. It is suggested that the presence of SIBO leads to an increase and persistence of disease symptoms but with a lower level of expression of the anti-inflammatory cytokine IL-10 in the blood serum; in addition, a positive correlation is determined between the

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webofjournals.com/index.php/5

duration of the IBS history and the presence of SIBO. According to E. Pyleris et al ., in patients with a confirmed diagnosis of IBS and SIBO, when examining an aspirate of the contents of the descending part of the duodenum in an amount greater than 10, the following microorganisms were determined: Escherichia coli (12.7%), Enterococcus spp (10.9%); other enterobacteria (18.2%); in the control group: Escherichia coli (3.1%), Enterococcus spp (6.1%). However, the problem of the combination of IBS and SIBO is also considered from another point of view. It is discussed that SIBO manifests itself with symptoms similar to those in IBS, but does not at all serve as a manifestation of this functional disease. Thus, with a combination of IBS and SIBO, there is an increase in the main complaints, but no new ones arise. Therefore, antibiotics prescribed for the treatment of SIBO in IBS are less effective, leading to a decrease in the intensity of symptoms than, for example, in the case of a combination of SIBO with diseases such as rosacea and scleroderma, when they are completely eliminated. The results of studies on the qualitative composition of microflora are contradictory, due to the lack of wide availability of adequate methods for its study. However, despite the inconsistency of the data provided, there is no doubt about the presence of significant differences in the intestinal microflora in patients with IBS and healthy volunteers.

It is possible that the change in microbiota in patients with IBS is associated with such factors as increased expression of signaling receptors responsible for the interaction of the host organism with bacterial cells; changes in the function of tight junctions between epithelial cells and impaired intestinal permeability; slow absorption of bile acids due to mutation of their transporter in the ileum; decreased expression of fibroblast growth factor 19 (FGF19). Under such conditions, opportunistic or pathogenic bacterial cells carrying adhesion factors gain an advantage over saprophytic microorganisms living in the intestinal lumen and, penetrating through the damaged epithelial barrier, interact with cells of the intestinal immune system. There is evidence that the gastrointestinal microflora, depending on the predominance of certain types of microorganisms, can also change intestinal permeability, affecting the expression of genes responsible for the synthesis of mucin. Thus, in the work of N. Singh et al . The effect of endogenous microflora on the expression of microRNA in the cecum of sterile mice and mice with normal microflora was studied. Presumably, microRNA affects 34 target genes encoding proteins responsible for the regulation of the intestinal barrier function: expression of tight junction proteins, glycosyltransferases , mucoproteins (responsible for the formation of mucin); immune regulation (MHC proteins type I and II). In mice with normal microflora, the expression of the studied genes was higher than in sterile animals. A few publications provide data on the correlation of individual clinical symptoms with the presence of certain species in the intestinal microbiota, but these data require clarification.

CONCLUSIONS

Thus, the above data largely support the primacy of microbiota changes and their impact on the barrier and immune function of the host organism, which may play an important role in the pathogenesis of IBS. For the first time in Uzbekistan, the structure of functional gastrointestinal diseases was studied in a multidisciplinary hospital and outpatient practice, as well as the frequency of erroneous diagnoses of functional gastrointestinal disease without proper

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webofjournals.com/index.php/5

examination. The 7x7 Questionnaire was developed and patented, the use of which in outpatient practice leads to an increase in the accuracy of determining the variant of functional gastrointestinal disease, which allows prescribing adequate treatment. For the first time, the fundamental role of changes in intestinal microbiota in the pathogenesis of functional gastrointestinal diseases was determined, as well as the relationship between microbiota disturbances and other pathogenetic mechanisms of symptom formation. The effectiveness of individual probiotic strains in reducing the severity of symptoms of functional gastrointestinal diseases was determined.

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