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РОЛЬ МИКРОБИОТЫ ЧЕЛОВЕКА В РАЗВИТИИ ВНУТРЕННИХ БОЛЕЗНЕЙ

Аннотация: *В статье рассмотрено значение микробиоты человека и результаты последних исследований, посвященных роли микробиоты человека в патогенезе внутренних заболеваний. Также включен обзор влияния антибиотиков на состав и функциональную активность микробиоты*.

Ключевые слова: Патофизиология внутренних болезней, микробиота человека, дисбактериоз, антибиотики, клиническая микробиология.

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THE ROLE OF HUMAN MICROBIOTA IN THE DEVELOPMENT OF INTERNAL DISEASES

Abstract: *This article reviews the significance of human microbiota and the results of recent studies dedicated to the role of human microbiota in the pathogenesis of internal diseases. It also includes a review of the effect of antibiotic drugs on the composition and functional activities of the microbiota.*

Key words: Pathophysiology of Internal diseases, human microbiota, dysbiosis, antibiotics, clinical microbiology.

Abstract

Microbiota contribute to body overall health. They contribute to body physiology and perform several functions. Also they are linked to the development of several diseases of different body systems. The pathogenetic link between microbiota and development of different diseases revolves around the imbalance in the composition of

microbiota (dysbiosis) which results in impairment of different significant functions of the microbiota, which leads to some pathological conditions that contribute significantly to the development of most internal diseases. Important to note, that these conditions aren't able individually to develop a disease, but they contribute in combination with other risk factors to develop a disease. The main pathological conditions that emerge during dysbiosis include: immune dysfunction, leaky gut syndrome, impaired metabolism of microbiota metabolites, and dietary products, production of proinflammatory agents, and production of other agents that disrupts body homeostasis. Antibiotics are one of the most important factors that cause dysbiosis, different antibiotic groups cause different amounts of damage on the composition and function of microbiota. The extent of this damage depends on factors such as the spectrum of antibiotic action, route of administration, dose and frequency of intake, age, overall health, and other factors.

Introduction

Human microbiota is a term used to refer to the microorganisms that inhabit the human body and take part in its vital activities. These microorganisms are crucial for human existence. They live inside the human body - on the mucosal surfaces, and within the lumen of the digestive system, and outside the body - on the skin. On this basis, they are classified into the microflora of the respiratory tract, microflora of the intestinal tract, microflora of the genitourinary tract, and microflora of the skin. The amount of human microbiota is very large, their number is estimated to be 10 times the total number of human body cells, as the number of human body cells is estimated at 10^{13} while human microbiota - at 10^{14}. The composition of human microbiota includes bacteria, yeast, protozoa, and viruses. Bacteria represent the most widespread organism among them. Human microbiota are involved in several body functions including: weight control, regulation of the immune system, synthesis of vitamins such as vitamin k and B12, food digestion, and detoxification. Generally, this article reviews the link between the human microbiota and the development of some internal diseases.

Human microbiota in pathology of internal diseases

Human microbiota are not only involved in body physiology, but also in its pathology. Dysbiosis, which is a persistent imbalance in the composition, and metabolic activities of the microbiome can lead to the development of several health problems such as obesity, cancer, immune dysfunction, cardiovascular disease, inflammatory bowel diseases, and others. Dysbiosis is caused by some health conditions such as inflammation and infections, diet with high amount of sugar and low amount of fibers, also can be caused by the intake of antibiotics, and by poor hygiene.

Inflammatory bowel diseases (IBD)

The exact cause of IBD is unclear yet. Studies propose the etiology of IBD to be linked to the following factors: genetic predisposition, immune dysregulation, environmental factors, and gut microbiota. Each of these factors are not sufficient individually for the development of IBD. Rather, the development of IBD requires the presence of all of these factors together, as each of them contributes a certain part of the pathogenesis of IBD. The factors related to microbiota that contribute to the development of IBD are the following:

Dysbiosis: studies revealed that patients with IBD often exhibit dysbiosis, which involves a decreased amount of beneficial bacteria and an increased amount of harmful bacteria. The altered microbial composition can disrupt the delicate balance between protective and harmful microorganisms

Impaired intestinal barrier functions (Leaky gut syndrome): Dysbiosis alters the function of microbiota as a protective intestinal barrier, because it prevents the interaction between microbiota and the intestinal epithelial cells. This dysfunction allows harmful substances to penetrate the intestinal mucosa, triggering an immune response and inflammation, and contributing to the development of IBD.

Immune dysregulation: Dysbiosis causes chronic altered immune response in the intestines, due to the change in microbiota composition, making the immune cells mistakenly attack the beneficial microbiota. This chronic immune dysregulation leads to damage in the intestinal tissue and establishes inflammation in IBD.

Production of pro-inflammatory molecules: dysbiosis causes increased production of pro-inflammatory factors, like cytokines and reactive oxygen-species. These molecules further contribute to the inflammation and intestinal damage in IBD.

Impaired production of metabolites: Another function of gut microbiota is represented by the anti-inflammatory action performed by various metabolites produced by the gut microbiota, an example of these metabolites include short-chain fatty acids (SCFAs), these metabolites help to maintain the gut health. During dysbiosis the production of these metabolites is decreased, which contributes to exacerbation of the inflammation and development of IBD.

It's important to note that while dysbiosis and the gut microbiota's role in IBD have been extensively studied, the exact mechanisms involved are complex and still not fully understood.

Cardiovascular diseases

Metabolism of dietary components: microbiota is involved in the breakdown of carbohydrates and fats, and processing of bile acids, where they convert primary bile acids into secondary bile acids. This function is disrupted during dysbiosis, which results in increased levels of lipids, particularly triglycerides and cholesterol, which are major risk factors for cardiovascular diseases such as atherosclerosis.

Trimethylamine N-oxide (TMAO) Production: During dysbiosis, harmful bacteria like some species of Clostridium and Proteus produce higher amounts of trimethylamine (TMA), the precursor of TMAO. TMAO is considered a pro-atherogenic metabolite. It contributes to atherosclerosis by several mechanisms: it inhibits cholesterol transport resulting in a higher level of circulating cholesterol. Also, TMAO disrupts platelets' function by increasing their responsiveness (making them hyperactive) which contributes to higher chance of thrombosis. Furthermore, TMAO promotes the activation of pro-inflammatory proteins such IL-6, COX-2, ICAM. All these factors lead to a higher chance of occurrence of major cardiovascular events, particularly CAD. Studies found a strong relation between TMAO levels and cardiovascular diseases.

SCFAs imbalance: as known, dysbiosis causes imbalance in SCFAs, this imbalance stimulates intestinal chromaffin to produce higher amounts of 5-hydroxytryptamine (5-HT) (Serotonin). 5-HT has the following actions: it inhibits the afferent signaling of intestinal vagus nerve, and affects the total peripheral resistance by causing vasoconstriction. Vasoconstriction results in high arterial pressure.

H2S deficiency: H2S has an important function in regulating blood pressure: it acts as a vasorelaxation agent, and stimulates angiogenesis. It also inhibits oxidative stress and inflammation. During dysbiosis, H2S production by microbiota decreases, contributing further to the development of hypertension.

Angiotensin II: as known, angiotensin is considered a potent vasoconstrictor agent. The production of angiotensin II during dysbiosis increases, mediated by the alteration of the immune response, which causes infiltration of immune cells in the vessels, resulting in general, in vascular dysfunction and arterial hypertension.

Respiratory diseases

Recent studies have shown a strong correlation between dysbiosis and the development of respiratory diseases. The results of the research revolve around the fact that changing the composition of human microbiota leads to a deterioration in the balance between harmful bacteria and beneficial bacteria, which contributes directly or indirectly to an increase in the possibility of respiratory infections as well as chronic respiratory diseases. Dysbiosis has been found in many studies to be present in patients with asthma, COPD, cystic fibrosis, bronchiectasis, and lung cancer.

Immune modulation: It’s clear now that microbiota contribute to the immune system of the whole body, and the respiratory system is one part of the body that is affected when dysbiosis occurs. During dysbiosis, immune dysregulation occurs, represented by hyper- or hypoactive immune response. Chronic immune impairment in the respiratory system contributes to chronic inflammation of the respiratory tract. Resulting in impaired mucociliary clearance mechanism, and compromise the integrity of the airway epithelium. This immune dysregulation contributes to increased susceptibility to respiratory infections, exacerbation and progression of chronic respiratory diseases. Understanding the correlation between dysbiosis and respiratory

diseases is crucial for developing targeted therapeutic strategies that aim to restore microbial balance and improve patient outcomes. In general, the studies dedicated to the role of microbiota in the development of respiratory diseases are still not enough to understand the complex mechanisms underlying dysbiosis-related respiratory diseases. Further research is needed to reveal the link between dysbiosis and respiratory diseases to explore the potential of microbiota-based interventions in their management.

Impact of antibiotics on human microbiota

Antibiotics use is well established by the treatment and prophylaxis of many bacterial infections, but unfortunately, it can affect the normal flora of the body. Which in general can cause diseases or exacerbate them. Due to its ability to alter the overall balance and diversity of microbiota which leads to metabolic alterations, increased gut susceptibility to colonization, and development of antibiotic resistance. The gut microbiota are the most susceptible to antibiotics, due to its exposure to orally administered antibiotics. This susceptibility arises from the fact that antibiotics are primarily absorbed in the intestines, leading to direct and prolonged contact with gut bacteria. Main factors that determine the range of antibiotic effects on the commensal microbiota include the spectrum range of antibiotics; broad-spectrum antibiotics have a more pronounced effects compared to narrow-spectrum antibiotics, the following classes affect the microbiota more than the other classes of antibiotics: amoxicillin-clavulanic, IV generation cephalosporins, and fluoroquinolones, these classes are known to target a wider range of bacteria, including beneficial ones, which contributes to the emergence of antibiotic-resistant strains. The dose, duration and frequency of antibiotic use; the higher the dose, and the more prolonged and repeated use of antibiotics, the more pronounced effects on our microbiota. Other factors include: drug delivery method, the individual's age, status of the immune system, overall health, and the baseline composition of microbiota, and the presence of pre-existing dysbiosis. Depending on these factors, antibiotics can cause short-term and long-term effects on human microbiota. Antibiotics in the short-term affect the colonization of normal microflora, as the colonization by beneficial bacteria decreases after the use of antibiotics, while the colonization by yeast S. Cerevisiae and bacterium C. difficile

increases. Also, they affect the total composition of normal flora, and cause functional and metabolic alterations, and harm the immune response, that is represented by the emergence of opportunistic infections. In the long-term, antibiotic resistance develops, recurrent infections by C. difficile occur, the microbial diversity decreases, and some species can even totally disappear.

List of literatures:

1. Patrick R. Murray, PhD, Ken S. Rosenthal, PhD, Michael A. Pfaller, MD, Medical Microbiology. Elsevier Health Sciences, 2015. 748 p.
1. Levinson W.E. Review of medical microbiology and immunology. McGraw Hill / Medical, 2016. 300 p.
2. John O. Oyewale, Oyewumi O. Oshamika, and Grace I. Olasehinde. The Human Microbiome and Its Impacts on Health. 2020 Jun 12. [Electronic resource] // https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7306068/ (access to 17.11.2023).
3. Hou K., Wu ZX., Chen XY. et al. Microbiota in health and diseases // Sig Transduct Target Ther 7. 2022. № 135.
4. Ramirez Jaime, Guarner Francisco, Bustos Fernandez Luis, Maruy Aldo, Sdepanian Vera Lucia, Cohen Henry. Antibiotics as Major Disruptors of Gut Microbiota. 2020. [Electronic resource] // https://www.frontiersin.org/articles/10.3389/fcimb.2020.572912 (access to 17.11.2023).
5. Patangia, D. V., Anthony Ryan, C., Dempsey, E., Paul Ross, R., & Stanton, C. Impact of antibiotics on the human microbiome and consequences for host health // MicrobiologyOpen, 11(1). e1260. https://doi.org/10.1002/mbo3.1260 (access to 17.11.2023).
6. Caroline H.M. How antibiotics affect your microbiome. 2019. April 17. [Electronic resource] // https://www.taconic.com/taconic-insights/microbiome-and-germ-free/antibiotics-affect-microbiome.html# (access to 17.11.2023).

7. Yue S., Mirae L., Eugene BC. The gut microbiome and inflammatory bowel diseases. 2022 Sep 23. [Electronic resource] // https://doi.org/10.1146%2Fannurev-med-042320-021020 (access to 17.11.2023).

8. Qiu Peng, Ishimoto Takatsugu, Fu Lingfeng, Zhang Jun, Zhang Zhenyong, Liu Yang, The Gut Microbiota in Inflammatory Bowel Disease, 2022. [Electronic resource] // https://www.frontiersin.org/articles/10.3389/fcimb.2022.733992 (access to 17.11.2023).

9. Jie Cai, Lulu Sun, Frank J. Gonzalez, Gut microbiota-derived bile acids in intestinal immunity, inflammation, and tumorigenesis. 2022. March 09. [Electronic resource] // https://doi.org/10.1016/j.chom.2022.02.004 (access to 17.11.2023).

10. Qiu, Peng and Ishimoto, Takatsugu and Fu, Lingfeng and Zhang, Jun and Zhang, Zhenyong and Liu, Yang, The Gut Microbiota in Inflammatory Bowel Disease, 2022. [Electronic resource] // https://www.frontiersin.org/articles/10.3389/fcimb.2022.733992 (access to 17.11.2023).

11. Gerald W. Tannock The Bowel Microbiota and Inflammatory Bowel Diseases // // International Journal of Inflammation, vol. 2010. [Electronic resource] // https://doi.org/10.4061/2010/954051 (access to 17.11.2023).

12. Yang, L., Bajinka, O., Jarju, P.O. et al. The varying effects of antibiotics on gut microbiota. [Electronic resource] // https://doi.org/10.1186/s13568-021-01274-w (access to 17.11.2023).

13. Novakovic M, Rout A, Kingsley T, Kirchoff R, Singh A, Verma V, Kant R, Chaudhary R. Role of gut microbiota in cardiovascular diseases // World J Cardiol. 2020. № 12(4). Pp. 110-122.

14. Chunxi, L., Haiyue, L., Yanxia, L., Jianbing, P., & Jin, S. The Gut Microbiota and Respiratory Diseases: New Evidence // Journal of immunology research, 2020. [Electronic resource] // https://doi.org/10.1155/2020/2340670 (access to 17.11.2023).

15. Li N., Dai Z., Wang Z. et al. Gut microbiota dysbiosis contributes to the development of chronic obstructive pulmonary disease. [Electronic resource] // https://doi.org/10.1186/s12931-021-01872-z (access to 17.11.2023).